



STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 192409

TO: Rei-Tsang Shiao
Location: rem/5A10/5C18
Art Unit: 1626
Monday, June 12, 2006
Case Serial Number: 10/788993

From: Saloni Sharma
Location: Biotech-Chem Library
REM-1A64
Phone: (571)272-8601

saloni.sharma@uspto.gov

Search Notes

Examiner Shiao,

See attached results.

If you have any questions about this search feel free to contact me at any time.

Thank you for using STIC search services!

Saloni Sharma
Technical Information Specialist
STIC Biotech/Chem Library
(571)272-8601

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JUL-9 2006

Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: Robert (Robby) Shiao Examiner #: 79521 Date: 06/09/2006
Art Unit: 1626 Phone Number: 2-0707 Serial Number: 10/788,993
Location (Bldg/Room#): REM (Mailbox #): 5A10 Results Format Preferred (circle): PAPER DISK

15C18

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: _____

Inventors (please provide full names): Madar et al.

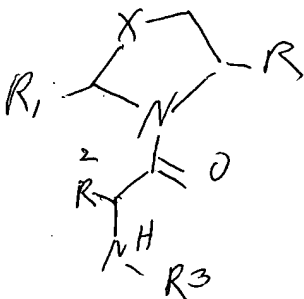
Earliest Priority Date: _____

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

I. search cpd 2 (see claim 1)



* R, R₁, R₂, R₃ are sub
* X is C,

II. search cpds of claim 6

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JUL-9 2006
SCIENTIFIC AND TECHNICAL INFORMATION CENTER (STIC)

STAFF USE ONLY

Searcher: Robert Shiao

Searcher Phone #: _____

Searcher Location: _____

Date Searcher Picked Up: 6/9/06

Date Completed: 6/12/06

Searcher Prep & Review Time: 40 min

Online Time: 35 min

Type of Search

____ NA Sequence (#)

____ AA Sequence (#)

____ Structure (#)

____ Bibliographic

____ Litigation

____ Fulltext

____ Other

Vendors and cost where applicable

☒ STN _____ Dialog

____ Questel/Orbit _____ Lexis/Nexis

____ Westlaw _____ WWW/Internet

____ In-house sequence systems

____ Commercial _____ Oligomer _____ Score/Length
____ Interference _____ SPDI _____ Encode/Transl

____ Other (specify)

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STIC SEARCH RESULTS FEEDBACK FORM

Biotech-Chem Library

Questions about the scope or the results of the search? Contact *the searcher* or contact:

Mary Hale, Information Branch Supervisor
Remsen Bldg. 01 D86
571-272-2507

Voluntary Results Feedback Form

> I am an examiner in Workgroup:

Example: 1610

> Relevant prior art found, search results used as follows:

- ☐ 102 rejection
- ☐ 103 rejection
- ☐ Cited as being of interest.
- ☐ Helped examiner better understand the invention.
- ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
(journal articles, conference proceedings, new product announcements etc.)

> Relevant prior art not found:

- ☐ Results verified the lack of relevant prior art (helped determine patentability).
- ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC-Biotech-Chem Library, Remsen Bldg.



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(FILE 'HOME' ENTERED AT 09:06:21 ON 12 JUN 2006)

FILE 'CAPLUS' ENTERED AT 09:07:52 ON 12 JUN 2006

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L1      28 SEA ABB=ON PLU=ON ("MADAR D J"/AU OR "MADAR DAVID"/AU OR
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E DJURIC S/AU
L2     184 SEA ABB=ON PLU=ON ("DJURIC S"/AU OR "DJURIC S W"/AU OR
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E MICHMERHUIZEN M/AU
L3      3 SEA ABB=ON PLU=ON ("MICHMERHUIZEN MELISSA"/AU OR "MICHMERHUIZ
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L5    32662 SEA ABB=ON PLU=ON LI X?/AU
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L6     25 SEA ABB=ON PLU=ON ("LONGENECKER K L"/AU OR "LONGENECKER
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L9    209 SEA ABB=ON PLU=ON ("SHAM H"/AU OR "SHAM H L"/AU OR "SHAM
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L11   52 SEA ABB=ON PLU=ON ("SZCZEPANKIEWICZ B G"/AU OR "SZCZEPANKIEWI
      CZ BRUCE"/AU OR "SZCZEPANKIEWICZ BRUCE G"/AU OR "SZCZEPANKIEWIC
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E WIEDEMAN P/AU
L12   50 SEA ABB=ON PLU=ON ("WIEDEMAN P"/AU OR "WIEDEMAN P E"/AU OR
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L18 12 SEA ABB=ON PLU=ON (L4 AND (L5 OR L6 OR L7 OR L8 OR L9 OR L10
OR L11 OR L12 OR L13))

L19 18 SEA ABB=ON PLU=ON (L5 AND (L6 OR L7 OR L8 OR L9 OR L10 OR
L11 OR L12 OR L13))

L20 9 SEA ABB=ON PLU=ON (L6 AND (L7 OR L8 OR L9 OR L10 OR L11 OR
L12 OR L13))

L21 26 SEA ABB=ON PLU=ON (L7 AND (L8 OR L9 OR L10 OR L11 OR L12 OR
L13))

L22 8 SEA ABB=ON PLU=ON (L8 AND (L9 OR L10 OR L11 OR L12 OR L13))

L23 39 SEA ABB=ON PLU=ON (L9 AND (L10 OR L11 OR L12 OR L13))

L24 8 SEA ABB=ON PLU=ON (L10 AND (L11 OR L12 OR L13))

L25 3 SEA ABB=ON PLU=ON (L11 AND (L12 OR L13))

L26 4 SEA ABB=ON PLU=ON (L12 AND L13)

L27 28 SEA ABB=ON PLU=ON (L15 AND (L16 OR L17 OR L18 OR L19 OR L20
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FILE 'STNGUIDE' ENTERED AT 09:22:13 ON 12 JUN 2006

FILE 'REGISTRY' ENTERED AT 09:42:31 ON 12 JUN 2006

L28 STRUCTURE UPLOADED

L29 STRUCTURE UPLOADED

L30 STRUCTURE UPLOADED

L31 0 SEA SSS SAM L30

L32 STRUCTURE UPLOADED

L33 50 SEA SSS SAM L32

L34 STRUCTURE UPLOADED

L35 50 SEA SSS SAM L34

FILE 'CAPLUS' ENTERED AT 09:48:44 ON 12 JUN 2006

E US2004-788993/APPS

L36 2 SEA ABB=ON PLU=ON (US2004-788993/AP OR US2004-788993/PRN)
D SCAN

FILE 'STNGUIDE' ENTERED AT 11:26:57 ON 12 JUN 2006

FILE 'REGISTRY' ENTERED AT 11:30:04 ON 12 JUN 2006

L37 STRUCTURE UPLOADED

L38 17 SEA SSS SAM L37

L39 456 SEA SSS FUL L37

FILE 'CAPLUS' ENTERED AT 11:34:00 ON 12 JUN 2006

L40 50 SEA ABB=ON PLU=ON L39

L41 21 SEA ABB=ON PLU=ON L40 NOT (PY>2002 OR AY>2002 OR PRY>2002)

L42 50 SEA ABB=ON PLU=ON (L36 OR L40)
D SCAN L36

L43 207996 SEA ABB=ON PLU=ON (DIABET?/OBI OR ANTI/OBI(2A)DIABETE?/OBI
OR INSULIN?/OBI)

L44 256730 SEA ABB=ON PLU=ON (DIABET? OR ANTI(2A)DIABETE? OR INSULIN?)/B
I
L45 7 SEA ABB=ON PLU=ON (L43 OR L44) AND L40
L46 23630 SEA ABB=ON PLU=ON ANTIDIABET?/BI,OBI
L47 6 SEA ABB=ON PLU=ON L46 AND L40
L48 7 SEA ABB=ON PLU=ON (L47 OR L45)
L49 28 SEA ABB=ON PLU=ON (L48 OR L41)
L50 28 SEA ABB=ON PLU=ON L40 AND P/DT
L51 44 SEA ABB=ON PLU=ON (L49 OR L50)
L52 41 SEA ABB=ON PLU=ON L51 NOT L27
L53 25 SEA ABB=ON PLU=ON L27 NOT L51

=> file caplus

FILE 'CAPLUS' ENTERED AT 11:43:10 ON 12 JUN 2006

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FILE COVERS 1907 - 12 Jun 2006 VOL 144 ISS 25

FILE LAST UPDATED: 11 Jun 2006 (20060611/ED)

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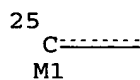
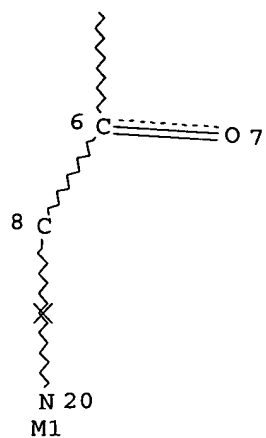
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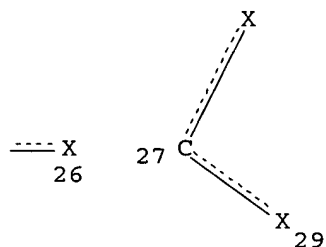
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L2 184 SEA FILE=CAPLUS ABB=ON PLU=ON ("DJURIC S"/AU OR "DJURIC S W"/AU OR "DJURIC STEVAN"/AU OR "DJURIC STEVAN W"/AU OR "DJURIC STEVAN WAKEFIELD"/AU OR "DJURIC STEVEN W"/AU OR "DJURIC STEVEN WAKEFIELD"/AU)
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L6 25 SEA FILE=CAPLUS ABB=ON PLU=ON ("LONGENECKER K L"/AU OR "LONGENECKER KENTON"/AU OR "LONGENECKER KENTON L"/AU OR "LONGENECKER KENTON LAMAR"/AU)
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L9 209 SEA FILE=CAPLUS ABB=ON PLU=ON ("SHAM H"/AU OR "SHAM H L"/AU OR "SHAM HING"/AU OR "SHAM HING L"/AU OR "SHAM HING LEUNG"/AU OR "SHAM HING LUENG"/AU)

L10 149 SEA FILE=CAPLUS ABB=ON PLU=ON ("STEWART K"/AU OR "STEWART K
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 L11 52 SEA FILE=CAPLUS ABB=ON PLU=ON ("SZCZEPANKIEWICZ B G"/AU OR
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 OR L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12 OR L13))
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 L18 12 SEA FILE=CAPLUS ABB=ON PLU=ON (L4 AND (L5 OR L6 OR L7 OR L8
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 L19 18 SEA FILE=CAPLUS ABB=ON PLU=ON (L5 AND (L6 OR L7 OR L8 OR L9
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 L20 9 SEA FILE=CAPLUS ABB=ON PLU=ON (L6 AND (L7 OR L8 OR L9 OR L10
 OR L11 OR L12 OR L13))
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 L11 OR L12 OR L13))
 L22 8 SEA FILE=CAPLUS ABB=ON PLU=ON (L8 AND (L9 OR L10 OR L11 OR
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 L26 4 SEA FILE=CAPLUS ABB=ON PLU=ON (L12 AND L13)
 L27 28 SEA FILE=CAPLUS ABB=ON PLU=ON (L15 AND (L16 OR L17 OR L18 OR
 L19 OR L20 OR L21 OR L22 OR L23 OR L24 OR L25 OR L26)) OR (L16
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 L25 OR L26)) OR (L22 AND (L23 OR L24 OR L25 OR L26)) OR (L23
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 L37 STR



Page 2-A



Page 2-B

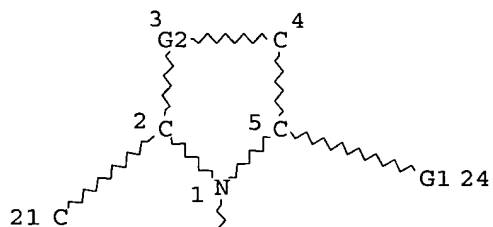
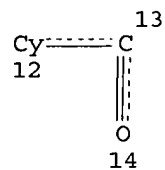
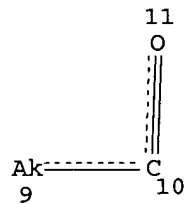
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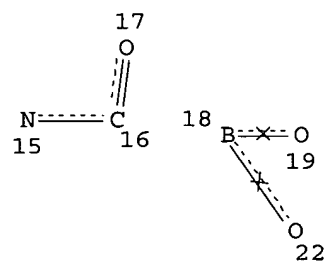
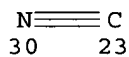
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| NSPEC | IS RC | AT | 21 |
| NSPEC | IS RC | AT | 22 |
| NSPEC | IS C | AT | 23 |

31 C M2



Page 1-A



28

Page 1-B

NSPEC IS C AT 24
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 DEFAULT MLEVEL IS ATOM
 MLEVEL IS CLASS AT 6 7 8 9 10 11 13 14 15 16 17 18 19 20 21 22 23
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 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 31

STEREO ATTRIBUTES: NONE

L39 456 SEA FILE=REGISTRY SSS FUL L37
 L40 50 SEA FILE=CAPLUS ABB=ON PLU=ON L39
 L41 21 SEA FILE=CAPLUS ABB=ON PLU=ON L40 NOT (PY>2002 OR AY>2002 OR
 PRY>2002)
 L43 207996 SEA FILE=CAPLUS ABB=ON PLU=ON (DIABET?/OBI OR ANTI/OBI(2A)DIA
 BETE?/OBI OR INSULIN?/OBI)
 L44 256730 SEA FILE=CAPLUS ABB=ON PLU=ON (DIABET? OR ANTI(2A)DIABETE?
 OR INSULIN?)/BI
 L45 7 SEA FILE=CAPLUS ABB=ON PLU=ON (L43 OR L44) AND L40
 L46 23630 SEA FILE=CAPLUS ABB=ON PLU=ON ANTIDIABET?/BI,OBI
 L47 6 SEA FILE=CAPLUS ABB=ON PLU=ON L46 AND L40
 L48 7 SEA FILE=CAPLUS ABB=ON PLU=ON (L47 OR L45)
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 L50 28 SEA FILE=CAPLUS ABB=ON PLU=ON L40 AND P/DT
 L51 44 SEA FILE=CAPLUS ABB=ON PLU=ON (L49 OR L50)
 L53 25 SEA FILE=CAPLUS ABB=ON PLU=ON L27 NOT L51

=> d ibib abs l53 tot

L53 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:492547 CAPLUS

TITLE: Crystal Structures of DPP-IV (CD26) from Rat Kidney
 Exhibit Flexible Accommodation of Peptidase-Selective
 Inhibitors

AUTHOR(S): Longenecker, Kenton L.; Stewart, Kent
 D.; Madar, David J.; Jakob, Clarissa
 G.; Fry, Elizabeth H.; Wilk, Sherwin; Lin, Chun W.;
 Ballaron, Stephen J.; Stashko, Michael A.; Lubben,
 Thomas H.; Yong, Hong; Pireh, Daisy
 ; Pei, Zhonghua; Basha, Fatima;
 Wiedeman, Paul E.; von Geldern, Thomas W.;
 Trevillyan, James M.; Stoll, Vincent S.

SOURCE: Biochemistry ACS ASAP
 CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Dipeptidyl peptidase IV (DPP-IV) belongs to a family of serine peptidases,
 and due to its indirect regulatory role in plasma glucose modulation,
 DPP-IV has become an attractive pharmaceutical target for diabetes
 therapy. DPP-IV inactivates the glucagon-like peptide (GLP-1) and several

other naturally produced bioactive peptides that contain preferentially a proline or alanine residue in the second amino acid sequence position by cleaving the N-terminal dipeptide. To elucidate the details of the active site for structure-based drug design, we crystallized a natural source preparation of DPP-IV isolated from rat kidney and determined its three-dimensional structure using X-ray diffraction techniques. With a high degree of similarity to structures of human DPP-IV, the active site architecture provides important details for the design of inhibitory compds., and structures of inhibitor-protein complexes offer detailed insight into three-dimensional structure-activity relationships that include a conformational change of Tyr548. Such accommodation is exemplified by the response to chemical substitution on 2-cyanopyrrolidine inhibitors at the 5 position, which conveys inhibitory selectivity for DPP-IV over closely related homologues. A similar conformational change is also observed in the complex with an unrelated synthetic inhibitor containing a xanthine core that is also selective for DPP-IV. These results suggest the conformational flexibility of Tyr548 is unique among protein family members and may be utilized in drug design to achieve peptidase selectivity.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:456711 CAPLUS

TITLE: Discovery, Structure-Activity Relationship, and Pharmacological Evaluation of (5-Substituted-pyrrolidinyl-2-carbonyl)-2-cyanopyrrolidines as Potent Dipeptidyl Peptidase IV Inhibitors

AUTHOR(S): **Pei, Zhonghua; Li, Xiaofeng; Longenecker, Kenton;** von Geldern, Thomas W.; **Wiedeman, Paul E.;** Lubben, Thomas H.; Zinker, Bradley A.; **Stewart, Kent;** Ballaron, Stephen J.; Stashko, Michael A.; Mika, Amanda K.; Beno, David W. A.; Long, Michelle; Wells, Heidi; Kempf-Grote, Anita J.; **Madar, David J.;** McDermott, Todd S.; Bhagavatula, Lakshmi; Fickes, Michael G.; **Pireh, Daisy;** Solomon, Larry R.; Lake, Marc R.; Edalji, Rohinton; Fry, Elizabeth H.; **Sham, Hing L.;** Trevillyan, James M.

CORPORATE SOURCE: Metabolic Disease Research, Advanced Technology, Departments of Exploratory Pharmacokinetics and Pharmaceuticals and Process Chemistry Global Pharmaceutical Research and Development, Abbott Laboratories, Abbott Park, IL, 60064-3500, USA

SOURCE: Journal of Medicinal Chemistry ACS ASAP
CODEN: JMCMAR; ISSN: 0022-2623 ~

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of (5-substituted pyrrolidinyl-2-carbonyl)-2-cyanopyrrolidine (C5-Pro-Pro) analogs was discovered as dipeptidyl peptidase IV (DPPIV) inhibitors as a potential treatment of diabetes and obesity. X-ray crystallog. data show that these inhibitors bind to the catalytic site of DPPIV with the cyano group forming a covalent bond with the serine residue of DPPIV. The C5-substituents make various interactions with the enzyme and affect potency, chemical stability, selectivity, and PK properties of the inhibitors. Optimized analogs are extremely potent with subnanomolar Ki's, are chemical stable, show very little potency decrease in the presence of plasma, and exhibit more than 1,000-fold selectivity against related

peptidases. The best compds. also possess good PK and are efficacious in lowering blood glucose in an oral glucose tolerance test in ZDF rats.

✓ REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1050874 CAPLUS

DOCUMENT NUMBER: 143:326207

TITLE: Preparation and pharmaceutical compositions of pyrrolidine derivatives as inhibitors of dipeptidyl peptidase-iv (DPP-iv)

INVENTOR(S): Akritopoulou-Zanze, Irini; Darczak, Daria; Dinges, Jurgen; Djuric, Stevan W.; Hoff, Ethan D.; Kopecka, Hana A.; Patel, Jyoti R.; Pei, Zhonghua; Shuai, Qi; Saris, Kathy; Sham, Hing L.; Wiedeman, Paul E.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 51 pp.

CODEN: USXXCO

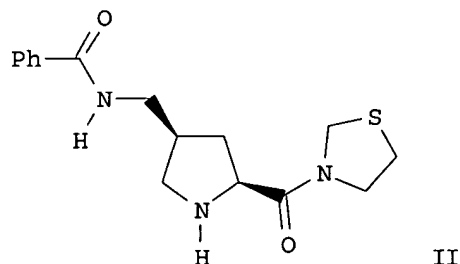
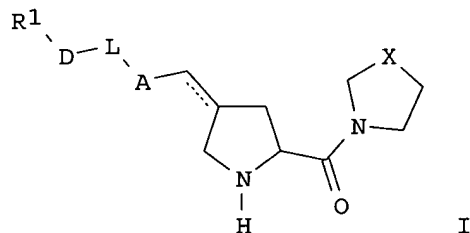
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|-------------------|----------|-----------------|----------|
| US 2005215603 | A1 | 20050929 | US 2004-795622 | 20040308 |
| PRIORITY APPLN. INFO.: | | | US 2004-795622 | 20040308 |
| OTHER SOURCE(S): | MARPAT 143:326207 | | | |
| GI | | | | |



AB Title compds. I [R1 = aryl, alkyl, cycloalkyl, etc.; D = CO, O, SO2, CONH, etc.; L = bond, -CH2-, aryl, etc; A = CO, NHSO2, NHCO, etc.; X = CHF, CH2,

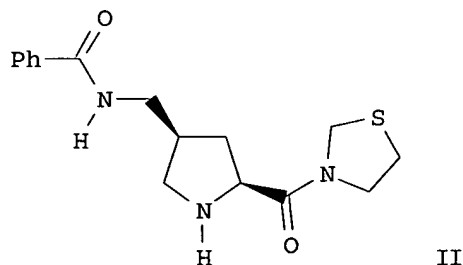
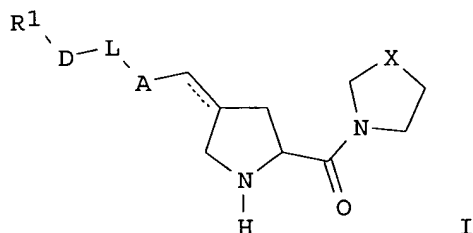
O, S, etc.], and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of dipeptidyl peptidase IV (DPP-IV). Thus, e.g., II was prepared by amidation of (2S,4R)-4-aminomethyl-2-(thiazolidine-3-carbonyl)pyrrolidine-1-carboxylic acid tert-Bu ester (preparation given) with benzoyl chloride. I were found to inhibit DPP-IV induced fluorescence with inhibitory consts. in a range of about 0.0005 μ M to about 7 μ M. I should prove useful for the prevention or treatment of diabetes, especially type II diabetes, as well as hyperglycemia, syndrome X, hyperinsulinemia, obesity, atherosclerosis, and various immunomodulatory diseases.

L53 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1028081 CAPLUS
 DOCUMENT NUMBER: 143:326202
 TITLE: Preparation and pharmaceutical compositions of pyrrolidine derivatives as inhibitors of dipeptidyl peptidase-iv (DPP-iv)
 INVENTOR(S): Akritopoulou-Zanze, Irini; Darczak, Daria; Dinges, Jurgan; Djuric, Stevan W.; Hoff, Ethan D.; Kopecka, Hana A.; Patel, Jyoti R.; Pei, Zhonghua; Shuai, Qi; Sarris, Kathy; Sham, Hing L.; Wiedeman, Paul E.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 50 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|-------------------|----------|-----------------|------------|
| US 2005209249 | A1 | 20050922 | US 2005-75319 | 20050308 |
| PRIORITY APPLN. INFO.: | | | US 2004-551079P | P 20040308 |
| OTHER SOURCE(S): | MARPAT 143:326202 | | | |

GI



AB Title compds. I [R1 = aryl, alkyl, cycloalkyl, etc.; D = CO, O, SO₂, CONH, etc.; L = bond, -CH₂-, aryl, etc; A = CO, NHSO₂, NHCO, etc.; X = CHF, CH₂, O, S, etc.], and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of dipeptidyl peptidase IV (DPP-IV). Thus, e.g., II was prepared by amidation of (2S,4R)-4-aminomethyl-2-(thiazolidine-3-carbonyl)pyrrolidine-1-carboxylic acid tert-Bu ester (preparation given) with benzoyl chloride. I were found to inhibit DPP-IV induced fluorescence with inhibitory consts. in a range of about 0.0005 μ M to about 7 μ M. I should prove useful for the prevention or treatment of diabetes, especially type II diabetes, as well as hyperglycemia, syndrome X, hyperinsulinemia, obesity, atherosclerosis, and various immunomodulatory diseases.

L53 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:739814 CAPLUS
 TITLE: Acyl thiazolidides-novel potent DPP-IV inhibitors
 AUTHOR(S): Shuai, Qi; Patel, Jyoti; Zanze, Irini; Dinges, Jorgen; Wiedeman, Paul E.; Pei, Zhonghua; Michmerhuizen, Melissa; Hoff, Ethan; Calvin, Douglas; Von Geldern, Thomas; Lubben, Tom; Ballaron, Steven; Stashko, Mike; Zinker, Brad; Djuric, Stevan W.; Beno, David; Kempf-Grote, Anita; Mika, Amanda; Farb, Tomas; Perham, Matthew; Adler, Andrew; Trevillyan, James; Sham, Hing L.
 CORPORATE SOURCE: Metabolic Disease Research, GPRD, Abbott Laboratories, Abbott Park, IL, 60064, USA
 SOURCE: Abstracts of Papers, 230th ACS National Meeting, Washington, DC, United States, Aug. 28-Sept. 1, 2005 (2005), MEDI-303. American Chemical Society: Washington, D. C.
 CODEN: 69HFCL
 DOCUMENT TYPE: Conference; Meeting Abstract; (computer optical disk)
 LANGUAGE: English

AB Dipeptidyl-peptidase IV (DPP-IV) is a serine peptidase that inactivates bioactive peptides such as GLP-1 by cleaving N-terminal dipeptides. Because GLP-1 is a peptide that can stimulate insulin secretion, inhibit glucagon incretion and promote proliferation of pancreatic beta cells, inhibitors of DPP-IV represent a potential treatment for type II diabetes by prohibiting the degradation of GLP-1 and extending the duration of action of GLP-1. We will discuss the discovery and SAR studies of the acyl thiazolidides as a novel class of DPP-IV inhibitors. The optimization of P1 and P2 sites of the acyl thiazolidides has lead to the discovery of very potent DPP-IV inhibitor such as 3a (K_{ic}=0.5 nM) and 1e (K_{ic}= 5 nM). 1e exhibits a 100-fold selectivity of DPP-IV over related serine proteases DPP7, DPP8, POP and FAP- α . The PK profile of 1e is promising (t_{1/2} = 5.0 h, F= 57.6%, V_{ss}=1.38 L/Kg, CL_p=1.94 L/h-Kg.). 1e has also shown a greater than 90% inhibition of DPP-IV activity in vivo at 3 mpk and 10 mpk, an increase in the active GLP-1 level and a 34% reduction of the glucose level (10 mpk) in an OGTT. The synthesis of acyl thiazolidide analogs and their in vitro and in vivo biol. data will be presented.

L53 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

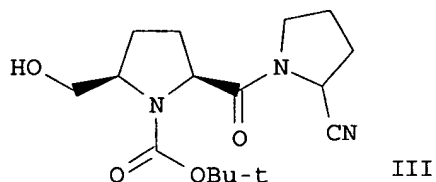
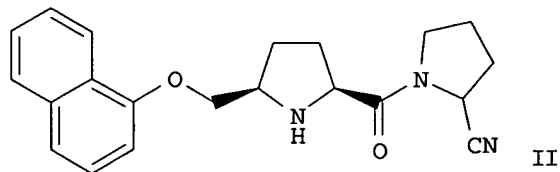
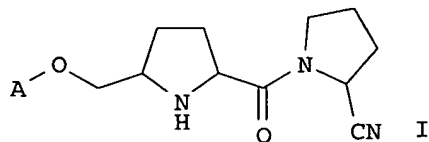
ACCESSION NUMBER: 2005:739812 CAPLUS
 TITLE: Discovery of potent DPP-IV inhibitors
 AUTHOR(S): Chen, Yixian; Richards, Steven; Shuai, Qi; Patel, Jyoti; Madar, David; Yong, Hong; Pei, Zhonghua; von Geldern, Thomas W.; Longenecker, Kenton L.; Stewart, Kent; Lubben, Tom; Ballaron, Steven; Stashko, Mike;

CORPORATE SOURCE: Trevillyan, James; **Sham, Hing**
Metabolic Disease Research Division, Abbott
Laboratories, Abbott Park, IL, 60064, USA
SOURCE: Abstracts of Papers, 230th ACS National Meeting,
Washington, DC, United States, Aug. 28-Sept. 1, 2005
(2005), MEDI-301. American Chemical Society:
Washington, D. C.
CODEN: 69HFCL
DOCUMENT TYPE: Conference; Meeting Abstract; (computer optical disk)
LANGUAGE: English
AB Small mol. inhibitors of DPP-IV have been proven to improve glucose
tolerance in diabetic patients. DPP-IV inhibition protects the incretin
GLP-1 from inactivation. GLP-1 stimulates insulin biosynthesis, inhibits
glucagon secretion and slows post-prandial gastric emptying. We have
discovered a series of proline based DPP-IV inhibitors with P2 sulfonamide
functionality. Earlier compds. in this series were potent inhibitors of
DPP-IV (IC₅₀ < 10 nM) but lost activity in the presence of plasma. The
sulfonamide groups were tolerated by the enzyme, and reduced the plasma
shift. We will discuss the synthesis and SAR of these compds., and
present the crystal structures of representative compds. bound to hDPP-IV.

L53 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:527399 CAPLUS
DOCUMENT NUMBER: 143:59815
TITLE: A preparation of L-prolylpyrrolidinecarbonitrile,
useful as inhibitors of dipeptidyl peptidase-IV
INVENTOR(S): **Pei, Zhonghua; Li, Xiaofeng;**
Longenecker, Kenton L.; Sham, Hing L.
; Wiedeman, Paul E.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 78 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--------|-----------|-----------------|------------|
| US 2005131019 | A1 | 20050616 | US 2004-935053 | 20040907 |
| PRIORITY APPLN. INFO.: | | | US 2003-500079P | P 20030904 |
| OTHER SOURCE(S): | MARPAT | 143:59815 | | |

GI



AB The invention relates to a preparation of L-prolylpyrrolidinecarbonitrile of formula I [wherein: A is a derivative of Ph, pyridine, quinoline], useful as inhibitors of dipeptidyl peptidase-IV (DPP-IV). For instance, L-prolylpyrrolidinecarbonitrile derivative II was prepared via etherification of 1-naphthol by (hydroxymethyl)pyrrolidine derivative III and subsequent N-cleavage. The invention compds. were found to inhibit DPP-IV induced fluorescence with inhibitory consts. in a range of about 0.0003 μM to about 0.03 μM .

L53 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:238948 CAPLUS

DOCUMENT NUMBER: 142:317078

TITLE: Preparation of pyrrolidine-2-carbonitrile derivatives and their use as inhibitors of dipeptidyl peptidase-IV (DPP-IV)

INVENTOR(S): Pei, Zhonghua; Li, Xiaofeng; Longenecker, Kenton L.; Sham, Hing L.; Wiedeman, Paul E.

PATENT ASSIGNEE(S): Abbott Laboratories, USA

SOURCE: PCT Int. Appl., 182 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2005023762 | A1 | 20050317 | WO 2004-US28886 | 20040907 |
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NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
 SN, TD, TG

PRIORITY APPLN. INFO.:

US 2003-655428

A 20030904

OTHER SOURCE(S):

MARPAT 142:317078

AB The invention relates to 1-(5-ROCH₂-substituted prolyl)pyrrolidine-2-carbonitriles (R is substituted Ph, 2-, 3-, or 4-pyridyl, or 4-quinolyl) or their pharmaceutically-acceptable salts or prodrugs, which inhibit dipeptidyl peptidase IV (DPP-IV) and are useful for the prevention or treatment of diabetes, especially type II diabetes, as well as hyperglycemia, syndrome X, hyperinsulinemia, β -cell failure, obesity, satiety disorders, atherosclerosis, and various immunomodulatory diseases. Thus, (2S)-1-[(5R)-5-[(4-carboxynaphthalen-1-yloxy)methyl]-L-prolyl]pyrrolidine-2-carbonitrile, prepared via N-acylation and etherification reactions, was evaluated for ability to treat diabetes using an acute oral glucose tolerance test (δ AUGC = 7,600 mg/mL/dL at 1.0 mg/kg vs. 9,900 mg/mL/dL for the control).

REFERENCE COUNT:

5

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:841814 CAPLUS

DOCUMENT NUMBER: 140:73029

TITLE: Identification of a monoacid-based, cell permeable, selective inhibitor of protein tyrosine phosphatase 1B
 AUTHOR(S): Xin, Zhili; Liu, Gang; Abad-Zapatero, Cele; **Pei, Zhonghua; Szczepankiewicz, Bruce G.; Li, Xiaofeng;** Zhang, Tianyuan; Hutchins, Charles W.; Hajduk, Philip J.; Ballaron, Stephen J.; Stashko, Michael A.; Lubben, Thomas H.; Trevillyan, James M.; Jirousek, Michael R.

CORPORATE SOURCE: Global Pharmaceutical Research and Development, Metabolic Disease Research, Abbott Laboratories, Abbott Park, IL, 60064-6098, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(22), 3947-3950

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 140:73029

AB Monoacid-based PTP1B inhibitors with improved physiochem. properties have been investigated. A (2-hydroxy-phenoxy) acetic acid-based phosphotyrosyl mimetic has been linked with an optimized second arylphosphate binding site ligand to produce a compound with low micromolar potency against PTP1B, good selectivity over TCPTP (20-fold) and high cell permeability in the Caco-2 system.

REFERENCE COUNT:

15

THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:52484 CAPLUS

DOCUMENT NUMBER: 139:188

TITLE: Potential drug targets and progress towards
 pharmacologic inhibition of hepatic glucose production

AUTHOR(S): Kurukulasuriya, R.; Link, J. T.; **Madar, D. J.**
; **Pei, Z.**; Richards, S. J.; Rohde, J. J.;
Souers, A. J.; **Szczepankiewicz, B. G.**
CORPORATE SOURCE: Metabolic Disease Research, Abbott Laboratories,
Abbott, Park, IL, 60064-6098, USA
SOURCE: Current Medicinal Chemistry (2003), 10(2), 123-153
CODEN: CMCHE7; ISSN: 0929-8673
PUBLISHER: Bentham Science Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. A number of therapeutic targets are currently under investigation for inhibition of hepatic glucose production with small mols. Antagonists of the glucagon receptor, glycogen phosphorylase, 11- β -hydroxysteroid dehydrogenase-1 and fructose 1,6-bisphosphatase are, or have been, under evaluation in human clin. trials. Other strategies, including glucocorticoid receptor antagonists and carnitine palmitoyltransferase inhibitors, are supported by proof of principle studies in man as well as rodents. Several potential targets including glucose-6-phosphatase, glucose-6-phosphatase translocase, glycogen synthase kinase-3, adenosine receptor 2B antagonists, phosphoenolpyruvate carboxykinase and pyruvate dehydrogenase kinase, have been validated by compds. that are effective in animal models. Other targets like PGC-1 α and CREB have initial validation support but no medicinal chemical has been reported.
✓ REFERENCE COUNT: 347 THERE ARE 347 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:52483 CAPLUS
DOCUMENT NUMBER: 139:16958
TITLE: Prospects for pharmacologic inhibition of hepatic glucose production
AUTHOR(S): Kurukulasuriya, R.; Link, J. T.; **Madar, D. J.**
; **Pei, Z.**; Rohde, J. J.; Richards, S. J.;
Souers, A. J.; **Szczepankiewicz, B. G.**
CORPORATE SOURCE: Metabolic Disease Research, Abbott Laboratories,
Abbott, Park, IL, 60064-6098, USA
SOURCE: Current Medicinal Chemistry (2003), 10(2), 99-121
CODEN: CMCHE7; ISSN: 0929-8673
PUBLISHER: Bentham Science Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Type 2 diabetes is a widespread disease where effective pharmacol. therapies can have a profound beneficial public health impact. Increased hepatic glucose production (HGP) is observed in diabetics and its moderation by currently available agents provides therapeutic benefits. This review describes the challenges associated with the discovery of small mols. that inhibit HGP. Gluconeogenesis, glycogenolysis, liver architecture, and hepatocyte composition are described to provide background information on hepatic function. Current methods of target validation for drug discovery, HGP measurement, diabetes animal models, as well as current drug therapies are covered. In the accompanying review article, the new drug targets being probed to produce the next generation of therapies are described. Significant pharmaceutical and academic efforts to pharmacol. inhibit HGP has the opportunity to provide new therapeutics for type 2 diabetics.
REFERENCE COUNT: 196 THERE ARE 196 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

✓ L53 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2002:869580 CAPLUS
 DOCUMENT NUMBER: 137:353320
 TITLE: Preparation of amino(oxo)acetic acid derivatives as selective protein tyrosine phosphatase inhibitors
 INVENTOR(S): Liu, Gang; Xin, Zhili; **Pei, Zhonghua; Li, Xiaofeng; Szczepankiewicz, Bruce G.**; Janowick, David A.; Oost, Thorsten K.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 60 pp., Cont.-in-part of U.S. Pat. Appl. 2002 72,516.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--------------------------|------|----------|-----------------|----------|
| US 2002169157 | A1 | 20021114 | US 2002-85157 | 20020227 |
| US 2002035137 | A1 | 20020321 | US 2001-918928 | 20010731 |
| US 2002072516 | A1 | 20020613 | US 2001-941471 | 20010829 |
| US 6972340 | B2 | 20051206 | | |
| WO 2003072537 | A2 | 20030904 | WO 2003-US3663 | 20030206 |
| WO 2003072537 | A3 | 20031218 | | |

W: CA, JP, MX

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR

PRIORITY APPLN. INFO.:
 US 2000-228651P P 20000829
 US 2000-650922 A2 20000829
 US 2001-918928 A2 20010731
 US 2001-941471 A2 20010829
 US 2002-85157 A 20020227

OTHER SOURCE(S): MARPAT 137:353320

AB Compds. B-L-A-N(D)COCO2P2 [A are rings of defined structure; B = H, alkyl, aryl, arylalkyl, heterocyclyl, or heterocyclylalkyl; D = substituted Ph, alkyl, or 1-alkenyl [the substituent at the o- or 2-position is alkoxy, alkyl, sulfamoyl, amino, cyano, nitro, CO2P1, SO3H, P(O)(OH)2, CH2P(O)(OH)2, CHFP(O)(OH)2, CF2P(O)(OH)2, or C(:NH)NH2] or certain 5-membered heterocycles; P1, P2 = H, alkyl, alkenyl, arylalkyl, cycloalkyl, cycloalkylalkyl; L = (un)substituted (hetero)alkylene] or their therapeutically acceptable salts were prepared as protein tyrosine kinase 1B (PTP1B) inhibitors. Thus, N-[5-[[N-acetyl-4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-3-ethylphenylalanyl]amino]pentanoyl]-L-methionine and Me 2-[4-[[N-acetyl-4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-3-ethylphenylalanyl]amino]butoxy]-6-hydroxybenzoate were prepared and showed Kic = 0.077 ± 0.012 and 0.016 ± 0.003 μM, resp., for inhibition of PTP1B.

✓ L53 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2002:730555 CAPLUS
 DOCUMENT NUMBER: 137:247920
 TITLE: Preparation of pyrrolidine neuraminidase inhibitors
 INVENTOR(S): Maring, Clarence J.; Gu, Yu Gui; Chen, Hui-Ju; Chen, Yuanwei; Degeoey, David A.; Flosi, William J.; Giranda, Vincent L.; Grampovnik, David J.; Kati, Warren M.; Kempf, Dale J.; Kennedy, April; Klein, Larry L.; Krueger, Allan C.; Lin, Zhen; Madigan, Darold L.;

McDaniel, Keith F.; Muchmore, Steven W.; **Sham, Hing L.**; **Stewart, Kent D.**; Stoll, Vincent S.; Sun, Minghua; Tu, Noah P.; Wagenaar, Frank L.; Wang, Gary T.; Wang, Sheldon; **Wiedeman, Paul E.**; Xu, Yibo; Yeung, Ming C.; Zhao, Chen; Hanessian, Stephen; Bayrakdarian, Malken; Luo, Xuehong
Abbott Laboratories, USA

PATENT ASSIGNEE(S):

SOURCE:

U.S., 253 pp., Cont.-in-part of U.S. Ser. No. 282,139, abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

2

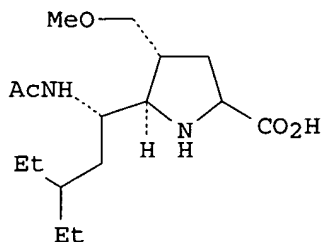
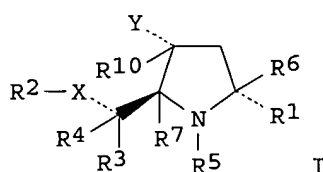
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| US 6455571 | B1 | 20020924 | US 1999-421787 | 19991019 |
| CA 2388859 | AA | 20010426 | CA 2000-2388859 | 20001010 |
| WO 2001028996 | A2 | 20010426 | WO 2000-US27910 | 20001010 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
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| JP 2003513889 | T2 | 20030415 | JP 2001-531796 | 20001010 |
| BR 2000010555 | A | 20030923 | BR 2000-10555 | 20001010 |
| EP 1358154 | A2 | 20031105 | EP 2000-972042 | 20001010 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| US 2004097471 | A1 | 20040520 | US 2002-253152 | 20020924 |
| US 6831096 | B2 | 20041214 | | |
| PRIORITY APPLN. INFO.: | | | US 1998-82828P | P 19980423 |
| | | | US 1999-282139 | B2 19990331 |
| | | | US 1999-421787 | A 19991019 |
| | | | WO 2000-US27910 | W 20001010 |

OTHER SOURCE(S):

MARPAT 137:247920

GI



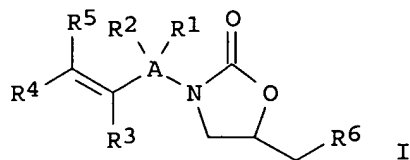
AB Pyrrolidines I [X = (un)substituted CONH, NHCO, CSNH, NHCS, NHSO₂, SO₂NH;
Y = H, (halo)alkyl, (halo)alkenyl, alkynyl, cycloalkyl(alkyl),

cycloalkenyl(alkyl), cycloalkenylalkenyl, (halo)phenyl, etc.; R1 = (CH₂)CO₂H, (CH₂)SO₃H, (CH₂)SO₂H, (CH₂)PO₃H₂, (CH₂)PO₂H, tetrazolyl(methyl), etc.; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, haloalkyl, or haloalkenyl; or R2X = (un)substituted heterocyclyl; R3, R4 = H, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, acyl, etc.; or R3R4C = carbocyclyl or heterocyclyl; R5 = H, alkynyl, cyclopropyl cyclobutyl, or (un)substituted Me, OH, acyl, imino, NH₂, etc.; R6, R7 = H, alkyl, alkenyl cycloalkyl(alkyl), cycloalkylalkenyl, cycloalkenyl(alkyl), cycloalkenylalkenyl, aryl(alkyl)arylalkenyl, heterocyclyl(alkyl), heterocyclylalkenyl; R10 = H, (cyclo)alkyl, (cyclo)alkenyl, fluoro], having relative or absolute configuration, were prepared as neuraminidase inhibitors for the treatment of diseases caused by microorganisms having a neuraminidase, especially influenza neuraminidase. For example, (±)-II•HCl was synthesized in an 11-step sequence involving (1) cycloaddn. of acrolein and t-Bu N-benzylglycinate to give (±)-(2S,3RS,5R)-1-benzyl-2-vinyl-3-formylpyrrolidine-5-carboxylic acid t-Bu ester (45%), (2) reduction of the aldehyde to the alc. (66%), (3) O-protection using t-butyldimethylsilyl chloride (71%), (4) oxidation of the vinyl group to an aldehyde (46%), (5) addition of 1-bromo-2-ethylbutane to the aldehyde (66%), (6) reductive amination of the ketone (64%), (7) amidation with AcOAc (72%), (8) deprotection of the alc. (61%), (9) etherification of the alc. with iodomethane, (10) N-deprotection (47%), and (11) deesterification and salt formation using 6N HCl. I inhibit influenza A and influenza B neuraminidase with K_i values for preferred compds. in the range 0.1 nM to 3.5 μM. In a cell culture plaque formation inhibition assay, I inhibited influenza virus A/N2/Tokyo in MDCK cells with EC₅₀ values between 100 μM and 1 nM; preferred compds. gave EC₅₀ values between 1 μM and 1 nM.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ✓ ANSWER 14 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2002:638287 CAPLUS
 DOCUMENT NUMBER: 137:185483
 TITLE: Preparation of oxazolidinones as antibacterial agents
 INVENTOR(S): **Wiedeman, Paul E.; Djuric, Steven W.**
 ; Pilushchev, Marina; Sciotti, Richard J.; **Madar, David J.; Kopecka, Hana**
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 30 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|-------------------|----------|-----------------|------------|
| US 2002115669 | A1 | 20020822 | US 2001-941806 | 20010829 |
| PRIORITY APPLN. INFO.: | | | US 2000-229239P | P 20000831 |
| OTHER SOURCE(S): | MARPAT 137:185483 | | | |
| GI | | | | |



AB Title compds. [I; A = Ph, substituted 5-membered aromatic ring containing 1-2 N,

O, S, or 6-membered aryl containing 1-2 N atoms; R1, R2 = H, alkyl, alkoxy, thioalkoxy, cycloalkyl, OH, amino, aminoalkyl, halo, haloalkyl, perfluoroalkyl; R3, R4, R5 = H, carboxamido, cyano, halo, NO2, perfluoroalkyl, (substituted) alkyl, alkanoyl, cycloalkyl, cyclothioalkoxy, cycloalkylsulfinyl, cycloalkoxycarbonyl, thioalkoxy, alkylsulfinyl, alkylsulfonyl, alkoxycarbonyl, cycloalkenyl, thiocycloalkenyl, cycloalkenylsulfinyl, cycloalkenylsulfonyl, aryl, aralkyl, arylthio, arylsulfinyl, arylsulfonyl, aryloxycarbonyl, heteroaryl, heteroarylalkyl, etc.; R6 = NHR7, N-phthalimido, NR7R8, NR8CO2R9, NR8CON(R8)2, OR9, SR9, SOR9, SO2R9; R7 = (substituted) alkanoyl, aryloyl, thioalkanoyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclylalkyl, etc.; R8 = H, (substituted) alkyl, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclylalkyl, protecting group; R9 = (substituted) alkyl, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, heteroarylalkyl, heterocycle, etc.] were prepared as antibacterial agents. N-[[[(5S)-3-[4-(2,2-dibromovinyl)-3-fluorophenyl]-2-oxo-1,3-oxazolidin-5-yl]methyl]acetamide, 5-acetyl-2-thienylboronic acid, tris(dibenzylideneacetone)dipalladium, and aqueous Na2CO3 in deoxygenated dimethoxyethane were heated at 55° for 20 h to give N-[[[(5S)-3-[4-[(Z)-2-(5-acetyl-2-thienyl)-2-bromoethenyl]-3-fluorophenyl]-2-oxo-1,3-oxazolidin-5-yl]methyl]acetamide. In an antibacterial activity assay, I inhibited the growth of Staphylococcus aureus, Staphylococcus epidermidis, Moraxella catarrhalis, Enterococcus faecium, and Streptococcus pneumoniae with MIC's in the range of about 0.125 µg/mL to about 128 µg/mL. I are also useful for treating psoriasis, arthritis, and toxicity due to chemotherapy (no data).

L53 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:522629 CAPLUS

DOCUMENT NUMBER: 137:93739

TITLE: Preparation of heterocyclyl-substituted oxazolidinones as antibacterial agents

INVENTOR(S): Madar, David J.; Pireh, Daisy;
Kopecka, Hana; Djuric, Stevan W.;
Wiedeman, Paul E.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 18 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--------|-----------|-----------------|------------|
| US 2002091107 | A1 | 20020711 | US 2001-949269 | 20010907 |
| PRIORITY APPLN. INFO.: | | | US 2000-231125P | P 20000908 |
| OTHER SOURCE(S): | MARPAT | 137:93739 | | |

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein ring A = Ph, or 5 or 6-membered aromatic ring containing

1-3 N, O, and S atoms; ring B = heterocycle; X = O, S, SO, SO₂, or NR₅; R₁ and R₂ = independently H, alkoxy, (halo)alkyl, NH₂, cycloalkyl, halo, OH, or perfluoroalkyl; R₃ = H, (halo)alkoxy, alkyl, NH₂, aryl, CN, halo, OH, or NO₂; R₄ = alkanoyl, alkoxycarbonyl, (hetero)aryl, amido, or (hetero)aryloyl; R₅ = H or (aryl)alkyl; and therapeutically acceptable salts thereof; with the proviso that R₄ ≠ Ph when ring B = 2,4-dioxo-1,3-thiazolidin-5-yl and X = O] were prepared for treating bacterial infections. For example, the N-(oxazolidinonylmethyl)acetamide (5S)-(Z)-II was prepared from N-[[[(5S)-3-(4-formylphenyl)-2-oxo-1,3-oxazolidin-5-yl]methyl]acetamide and 4,5-dimethyl-1,3-dihydro-2H-indol-2-one in EtOH at the presence of piperidine. I inhibited the growth of bacteria such as staphylococcus aureus, staphylococcus epidermidis, moraxella catarrhalis, enterococcus faecium, and streptococcus pneumoniae in the range of 2µg/mL to 128 µg/mL. I are also useful for treating psoriasis, arthritis, and toxicity due to chemotherapy (no data).

L53 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:185111 CAPLUS

DOCUMENT NUMBER: 136:247568

TITLE: Preparation of oxazolidinones as antibacterial agents

INVENTOR(S): Madar, David J.; Pireh, Daisy;
Kopecka, Hana; Djuric, Steven W.;
Wiedeman, Paul E.

PATENT ASSIGNEE(S): Abbott Laboratories, USA

SOURCE: PCT Int. Appl., 42 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| ----- | ---- | ----- | ----- | ----- |
| WO 2002020515 | A1 | 20020314 | WO 2001-US28125 | 20010907 |

W: CA, JP, MX

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,

PT, SE, TR

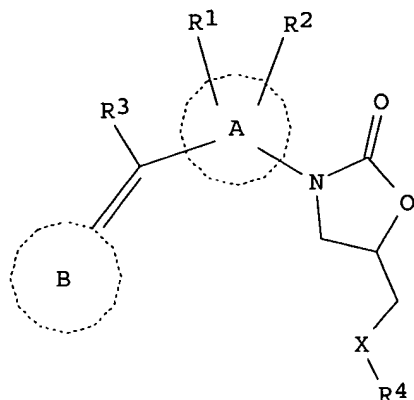
PRIORITY APPLN. INFO.:

US 2000-658003

A 20000908

OTHER SOURCE(S): MARPAT 136:247568

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I

AB The preparation of oxazolidinones [I; wherein A = Ph, five- or six-membered ring containing 1-3 atoms selected from N, O, and S; B = heterocycle; X = O, S, S(O), SO₂, and NR₅ (where R₅ = H, alkyl, arylalkyl); R₁, R₂, independently = H, alkoxy, alkyl, amino, cycloalkyl, halo, etc.; R₃ = H, alkoxy, alkyl, amino aryl, etc.; R₄ = alkanoyl, alkoxycarbonyl, amido, aryl, etc.] is described. Thus, a multistep synthesis of N-[[[(5S)-3-[3-fluoro-4-[(E)-[2-oxo-1,2-dihydro-3H-pyrrolo(2,3-b)pyridin-3-ylidene)methyl]phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl]acetamide is given. The prepared compds. are useful as, inter alia, antibacterial agents, inhibiting the growth of bacteria with min. inhibitory concns. in a range of about 2 µg/mL to about 8 µg/mL.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 17 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:171870 CAPLUS

DOCUMENT NUMBER: 136:216743

TITLE: Preparation of oxazolidinones as antibacterial agents

INVENTOR(S): Wiedeman, Paul E.; Djuric, Stevan W.
; Pliushchev, Marina; Sciotti, Richard J.; Madar,
David J.; Kopecka, Hana

PATENT ASSIGNEE(S): Abbott Laboratories, USA

SOURCE: PCT Int. Appl., 69 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

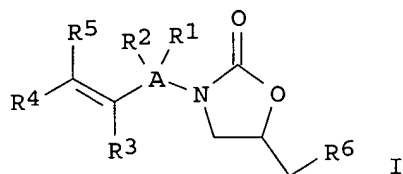
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2002018354 | A1 | 20020307 | WO 2001-US26883 | 20010829 |
| WO 2002018354 | C1 | 20020704 | | |
| W: CA, JP, MX | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | |

PRIORITY APPLN. INFO.: US 2000-652332 A 20000831

OTHER SOURCE(S): MARPAT 136:216743

GI



AB Title compds. [I; A = Ph , substituted 5-membered aromatic ring containing 1-2 N,

O, S, or 6-membered aryl containing 1-2 N atoms; R1, R2 = H, alkyl, alkoxy, thioalkoxy, cycloalkyl, OH, amino, aminoalkyl, halo, haloalkyl, perfluoroalkyl; R3, R4, R5 = H, carboxamido, cyano, halo, NO2, perfluoroalkyl, (substituted) alkyl, alkanoyl, cycloalkyl, cyclothioalkoxy, cycloalkylsulfinyl, cycloalkoxycarbonyl, thioalkoxy, alkylsulfinyl, alkylsulfonyl, alkoxycarbonyl, cycloalkenyl, thiocycloalkenyl, cycloalkenylsulfinyl, cycloalkenylsulfonyl, aryl, aralkyl, arylthio, arylsulfinyl, arylsulfonyl, aryloxycarbonyl, heteroaryl, heteroarylalkyl, etc.; R6 = NHR7, N-phthalimido, NR7R8, NR8CO2R9, NR8CON(R8)2, OR9, SR9, SOR9, SO2R9; R7 = (substituted) alkanoyl, aryloyl, thioalkanoyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclalkyl, etc.; R8 = H, (substituted) alkyl, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclalkyl, protecting group; R9 = (substituted) alkyl, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, heteroarylalkyl, heterocycle, etc.], were prepared as antibacterials (no data). N-[[[(5S)-3-[4-(2,2-dibromovinyl)-3-fluorophenyl]-2-oxo-1,3-oxazolidin-5-yl]methyl]acetamide, 5-acetyl-2-thienylboronic acid, tris(dibenzylideneacetone)dipalladium, and aqueous Na2CO3 in deoxygenated dimethoxyethane were heated at 55° for 20 h to give N-[[[(5S)-3-[4-[(Z)-2-(5-acetyl-2-thienyl)-2-bromoethenyl]-3-fluorophenyl]-2-oxo-1,3-oxazolidin-5-yl]methyl]acetamide.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:851793 CAPLUS

DOCUMENT NUMBER: 136:5986

TITLE: Preparation of azole inhibitors of cytokine production

INVENTOR(S): Bamaung, Nwe Y.; Basha, Anwer; **Djuric, Stevan W.**; Gubbins, Earl J.; Luly, Jay R.; Tu, Noah P.; **Madar, David J.**; Warrior, Usha; **Wiedeman, Paul E.**; Zhou, Xun; Sciotti, Richard J.; Wagenaar, Frank L.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 124 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

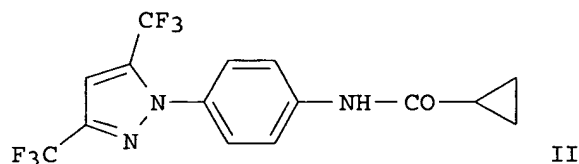
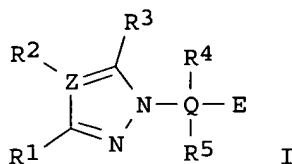
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| US 2001044445 | A1 | 20011122 | US 1999-289155 | 19990408 |
| PRIORITY APPLN. INFO.: | | | US 1999-289155 | 19990408 |

OTHER SOURCE(S): MARPAT 136:5986
GI



AB The title compds. [I; R1, R3 = H, aryl, perfluoroalkyl, etc.; Z = N, C; R2 is absent or = H, alkyl, cycloalkyl, etc.; Q = (hetero)aryl (when Q = Ph, the Ph is 2-, 3-, or 4-substituted by E relative to the position of attachment of the pyrazole or 1,2,4-triazole ring to the Ph ring); R4, R5 = H, alkyl, haloalkyl, etc.; E = NO₂, NH₂, etc.], useful for inhibiting cytokine (Interleukin-2, Interleukin-4, or Interleukin-5) production and cellular proliferation in stimulated human T cell lines or human peripheral blood mononuclear cells (biol. data given) and therefore have utility in the treatment of diseases that are prevented by or ameliorated with cytokine inhibitors, were prepared General procedures for preparation of compds. I were described. Thus, the title compound II was prepared

L53 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:639826 CAPLUS

TITLE: 3,5-Bis(trifluoromethyl)pyrazoles: A novel class of NFAT transcription factor regulator

AUTHOR(S): Madar, David J.; Djuric, Stevan W.

; BaMaung, Nwe Y.; Basha, Anwer; Liu, Huaqing; Luly, Jay R.; Sciotti, Richard J.; Tu, Noah P.; Wagenaar, Frank L.; Wiedeman, Paul E.; Zhou, Xun; Ballaron, Stephen; Bauch, Joy; Chen, Yung-Wu; Chiou, X. Grace; Fey, Thomas; Gauvin, Donna; Gubbins, Earl; Hsieh, Gin C.; Marsh, Kennan C.; Mollison, Karl W.; Pong, Melissa; Shaughnessy, Thomas K.; Sheets, Michael P.; Smith, Morey; Trevillyan, James M.; Warrior, Usha; Wegner, Craig D.; Carter, George W.

CORPORATE SOURCE: Infectious Disease Research, Abbott Laboratories, Abbott Park, IL, 60064-6217, USA

SOURCE: Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26-30, 2001 (2001), MEDI-007. American Chemical Society: Washington, D. C.

CODEN: 69BUZP

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB A series of bis(trifluoromethyl)pyrazoles (BTPs) has been found to be a novel inhibitor of cytokine production. Identified initially as inhibitors of IL-2 synthesis, the BTPs have been optimized in this regard and even inhibit IL-2 production with a 10-fold enhancement over cyclosporine in an ex vivo assay. Addnl., the BTPs show inhibition of IL-4, IL-5, IL-8, and eotaxin production. Unlike the IL-2 inhibitors, cyclosporine and FK506, the BTPs do not directly inhibit the dephosphorylation of NFAT by calcineurin. The SAR of several subclasses of the BTPs will be discussed. Also, expts. which shed light on the mechanism of action of this series will be highlighted.

L53 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:372448 CAPLUS

DOCUMENT NUMBER: 135:152741

TITLE: Synthesis of N-arylated oxazolidinones via a palladium catalyzed cross coupling reaction. Application to the synthesis of the antibacterial agent Dup-721

AUTHOR(S): **Madar, D. J.; Kopecka, H.; Pireh, D.;** Pease, J.; Pliushchev, M.; Sciotti, R. J.; **Wiedeman, P. E.; Djuric, S. W.**

CORPORATE SOURCE: Infectious Disease and Process Chemistry Research, Abbott Laboratories, Abbott Park, IL, 60064-6217, USA

SOURCE: Tetrahedron Letters (2001), 42(22), 3681-3684

CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 135:152741

AB A method for the intermol. coupling of aryl bromides and oxazolidinones is described. Application to intermediates useful for the preparation of a known class of antibacterial agent and the synthesis of the known antibacterial oxazolidinone Dup-721 are described.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:300677 CAPLUS

DOCUMENT NUMBER: 134:326397

TITLE: Preparation of pyrrolidine neuraminidase inhibitors

INVENTOR(S): Maring, Clarence J.; Giranda, Vincent L.; Kempf, Dale J.; Stoll, Vincent S.; Sun, Minghua; Zhao, Chen; Gu, Yu Gui; Hanessian, Stephen; Wang, Gary T.; Krueger, Allan C.; Chen, Hui-ju; Chen, Yuanwei; Degoe, David A.; Flosi, William J.; Grampovnik, David J.; Kati, Warren M.; Kennedy, April L.; Klein, Larry L.; Lin, Zhen; Madigan, Darold L.; Mcdaniel, Keith F.; Muchmore, Steven W.; **Sham, Hing L.; Stewart, Kent D.**; Tu, Noah P.; Wagenaar, Frank L.; Wang, Sheldon; **Wiedeman, Paul E.**; Xu, Yibo; Yeung, Ming C.; Bayrakdarian, Malken; Luo, Xuehong

PATENT ASSIGNEE(S): Abbott Laboratories, USA

SOURCE: PCT Int. Appl., 714 pp.

CODEN: PIXXD2

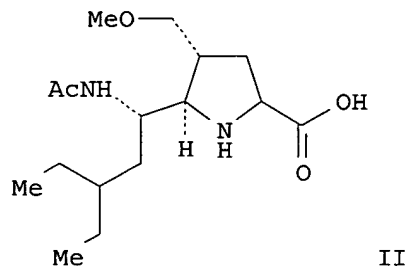
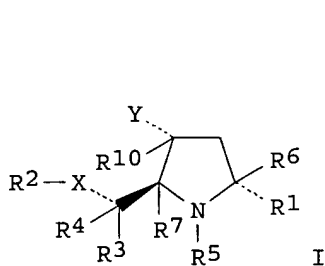
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|-------------|
| WO 2001028996 | A2 | 20010426 | WO 2000-US27910 | 20001010 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| US 6455571 | B1 | 20020924 | US 1999-421787 | 19991019 |
| CA 2388859 | AA | 20010426 | CA 2000-2388859 | 20001010 |
| JP 2003513889 | T2 | 20030415 | JP 2001-531796 | 20001010 |
| BR 2000010555 | A | 20030923 | BR 2000-10555 | 20001010 |
| EP 1358154 | A2 | 20031105 | EP 2000-972042 | 20001010 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | |
| PRIORITY APPLN. INFO.: | | | US 1999-421787 | A 19991019 |
| | | | US 1998-82828P | P 19980423 |
| | | | US 1999-282139 | B2 19990331 |
| | | | WO 2000-US27910 | W 20001010 |
| OTHER SOURCE(S): | MARPAT 134:326397 | | | |
| GI | | | | |



AB Title compds. (I) [wherein X = (un)substituted CONH, NH, CSNH, NHCS, NHSO₂, SO₂NH; Y = H, (halo)alkyl, (halo)alkenyl, alkynyl, cycloalkyl(alkyl), cycloalkenyl(alkyl), cycloalkenylalkenyl, (halo)phenyl, N(O):CHCH₃, halo, heterocyclyl, or (un)substituted (CH₂)nOH, CH(OH)CH₂(OH), (CH₂)nSH, (CH₂)nCN, (CH₂)nN₃, (CH₂)nNH₂, etc.; n = 0-2; R₁ = (CH₂)CO₂H, (CH₂)SO₃H, (CH₂)SO₂H, (CH₂)PO₃H₂, (CH₂)PO₂H, tetrazolyl(methyl), (CH₂)CONHSO₂R₁₁, or (un)substituted (CH₂)SO₂NH₂; R₁₁ = alkyl, alkenyl, cycloalkyl(alkyl), cycloalkenyl(alkyl), cycloalkenylalkenyl, aryl(alkyl), arylalkenyl, heterocyclyl(alkyl), or heterocyclylalkenyl; R₂ = H, (cyclo)alkyl, (cyclo)alkenyl, haloalkyl, or haloalkenyl; or R₂X = (un)substituted heterocyclyl; R₃ and R₄ = independently H, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, or (un)substituted ketones, acids, amides, alc., thiols, etc.; or R₃ and R₄ taken together with the C to which they are attached form a carbocyclic or heterocyclic ring; R₅ = H, alkynyl, cyclopropyl cyclobutyl, or (un)substituted Me, OH, acyl, imino, NH₂, etc.; R₆ and R₇ = independently H, alkyl, alkenyl cycloalkyl(alkyl), cycloalkylalkenyl, cycloalkenyl(alkyl), cycloalkenylalkenyl, aryl(alkyl)arylalkenyl,

heterocyclyl(alkyl), or heterocyclylalkenyl; R10 = H, (cyclo)alkyl, (cyclo)alkenyl, or fluoro] were prepared as neuraminidase inhibitors for the treatment of diseases caused by microorganisms having a neuraminidase, especially influenza neuraminidase. For example, (\pm)-II•HCl was synthesized in an 11-step sequence involving (1) cycloaddn. of acrolein and t-Bu N-benzylglycinate to give (\pm)-(2S,3RS,5R)-1-benzyl-2-vinyl-3-formylpyrrolidine-5-carboxylic acid t-Bu ester (45%), (2) reduction of the aldehyde to the alc. (66%), (3) O-protection using t-butyldimethylsilyl chloride (71%), (4) oxidation of the vinyl group to an aldehyde (46%), (5) addition of 1-bromo-2-ethylbutane to the aldehyde (66%), (6) reductive amination of the ketone (64%), (7) amidation with AcOAc (72%), (8) deprotection of the alc. (61%), (9) etherification of the alc. with iodomethane, (10) N-deprotection (47%), and (11) deesterification and salt formation using 6N HCl. I inhibit influenza A and influenza B neuraminidase with Ki values between 0.1 nM and 700 μ M; Ki values for preferred compds. ranged from 0.1 nM to 3.5 μ M. In a cell culture plaque formation inhibition assay, I inhibited influenza virus A/N2/Tokyo in MDCK cells with EC50 values between 100 μ M and 1 nM; preferred compds. gave EC50 values between 1 μ M and 1 nM.

✓ L53 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:500185 CAPLUS

DOCUMENT NUMBER: 133:202593

TITLE: 3,5-Bis(trifluoromethyl)pyrazoles: A Novel Class of NFAT Transcription Factor Regulator

AUTHOR(S): Djuric, Stevan W.; BaMaung, Nwe Y.; Basha, Anwer; Liu, Huaqing; Luly, Jay R.; Madar, David J.; Sciotti, Richard J.; Tu, Noah P.; Wagenaar, Frank L.; Wiedeman, Paul E.; Zhou, Xun; Ballaron, Stephen; Bauch, Joy; Chen, Yung-Wu; Chiou, X. Grace; Fey, Thomas; Gauvin, Donna; Gubbins, Earl; Hsieh, Gin C.; Marsh, Kennan C.; Mollison, Karl W.; Pong, Melissa; Shaughnessy, Thomas K.; Sheets, Michael P.; Smith, Morey; Trevillyan, James M.; Warrior, Usha; Wegner, Craig D.; Carter, George W.

CORPORATE SOURCE: Immunological Diseases Research, Abbott Laboratories, Abbott Park, IL, 60064-6217, USA

SOURCE: Journal of Medicinal Chemistry (2000), 43(16), 2975-2981

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

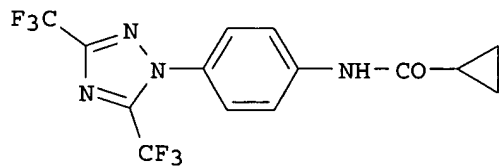
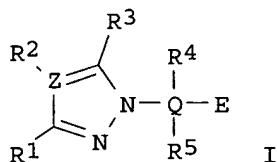
AB The authors describe the identification and characterization of a novel series of NFAT regulators that exert their biol. effects via a mechanism that does not involve inhibition of the Ca-dependent phosphatase calcineurin. A series of bis(trifluoromethyl)pyrazoles (BTPs) has been a novel inhibitor of cytokine production. Identified initially as inhibitors of IL-2 synthesis, the BTPs have been optimized in this regard and even inhibit IL-2 production with a 10-fold enhancement over cyclosporine in an ex vivo assay. Addnl., the BTPs show inhibition of IL-4, IL-5, IL-8, and eotaxin production. Unlike the IL-2 inhibitors, cyclosporine and FK506, the BTPs do not directly inhibit the dephosphorylation of NFAT by calcineurin. Structure-activity relations are briefly discussed. Pharmacokinetic data showed that the BTPs are extensively protein bound.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:659365 CAPLUS
 DOCUMENT NUMBER: 131:271873
 TITLE: Preparation of pyrazoles and triazoles as inhibitors of cytokine production
 INVENTOR(S): Ba Maung, Nwe Y.; Basha, Anwer; Djuric, Stevan W.; Gubbins, Earl J.; Luly, Jay R.; Tu, Noah P.; Madar, David J.; Warrior, Usha; Wiedeman, Paul E.; Zhou, Xun; Wagenaar, Frank L.; Sciotti, Richard J.
 PATENT ASSIGNEE(S): Abbott Laboratories, USA
 SOURCE: PCT Int. Appl., 319 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-------------------|------------|
| WO 9951580 | A1 | 19991014 | WO 1999-US7766 | 19990408 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2327185 | AA | 19991014 | CA 1999-2327185 | 19990408 |
| AU 9933879 | A1 | 19991025 | AU 1999-33879 | 19990408 |
| EP 1068187 | A1 | 20010117 | EP 1999-915341 | 19990408 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| JP 2002510679 | T2 | 20020409 | JP 2000-542301 | 19990408 |
| PRIORITY APPLN. INFO.: | | | US 1998-56996 | A 19980408 |
| | | | WO 1999-US7766 | W 19990408 |
| OTHER SOURCE(S): | | | MARPAT 131:271873 | |
| GI | | | | |



AB Title compds. [I; R1 = H, NH₂, OCONH₂, CN, NO₂, OH, CO₂H, F, Cl, Br, I, aryl, perfluoroalkyl, heterocyclyloxy, heterocyclylsulfonyl; R2 = H, alkyl cycloalkyl, alkylcarbonyl, heterocyclyl; R3 = H, NH₂, OCONH₂, CN, NO₂, OH, CO₂H, F, Cl, Br, I, aryl, perfluoroalkyl, heterocyclyloxy, heterocyclylsulfonyl; R4 and R5 are independently selected from H, alkyl, alkoxy, halo, perfluoroalkyl, CN, heterocycle; E = LB; B = alkyl, alkenyl, alkynyl; L = N:N, N:CH, CH:N, ON:CH, O, CO, NH, NHCO, NHSO₂, NHCH₂, alkenylene; Q = benzene ring with 2, 3, or 4 substituted E, heterocycle; Z = C; R2Z = N], E, Z isomers, stereoisomers, pharmaceutical acceptable salts, and prodrugs are prepared and tested as cytokine production inhibitors and are useful for treating diseases that are prevented by or ameliorated with Interleukin-2, Interleukin-4, or Interleukin-5 production inhibitors. Thus, the title compound II was prepared

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LE3 ANSWER 24 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:191130 CAPLUS

DOCUMENT NUMBER: 131:39198

TITLE: Inhibition of p56lck tyrosine kinase by isothiazolones

AUTHOR(S): Trevillyan, James M.; Chiou, X. Grace; Ballaron, Stephen J.; Tang, Qing M.; Buko, Alex; Sheets, Michael P.; Smith, Morey L.; Putman, C. Brent; **Wiedeman, Paul**; Tu, Noah; **Madar, David**; Smith, Harriet T.; Gubbins, Earl J.; Warrior, Usha P.; Chen, Yung-Wu; Mollison, Karl W.; Faltynek, Connie R.; **Djuric, Stevan W.**

CORPORATE SOURCE: Abbott Laboratories, Immunological Disease Research, Abbott Park, IL, 60064-6119, USA

SOURCE: Archives of Biochemistry and Biophysics (1999), 364(1), 19-29

CODEN: ABBIA4; ISSN: 0003-9861

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Lck encodes a 56-kDa protein-tyrosine kinase, predominantly expressed in T lymphocytes, crucial for initiating T cell antigen receptor (TCR) signal transduction pathways, culminating in T cell cytokine gene expression and effector functions. As a consequence of a high-throughput screen for selective, novel inhibitors of p56lck, an isothiazolone compound was identified, methyl-3-(N-isothiazolone)-2-thiophenecarboxylate (A-125800), which inhibits p56lck kinase activity with IC₅₀ = 1-7 μM. Under similar assay conditions, the isothiazolone compound was equipotent in blocking the ZAP-70 tyrosine kinase activity but was 50 to 100 times less potent against the catalytic activities of p38 MAP kinase and c-Jun N-terminal kinase 2α. A-125800 blocked activation-dependent TCR tyrosine phosphorylation and intracellular calcium mobilization in Jurkat T cells (IC₅₀ = 35 μM) and blocked T cell proliferation in response to alloantigen (IC₅₀ = 14 μM) and CD3/CD28-induced IL-2 secretion (IC₅₀ = 2.2 μM) in primary T cell cultures. Inhibition of p56lck by A-125800 was dose- and time-dependent and was irreversible. A substitution of methylene for the sulfur atom in the isothiazolone ring of the compound completely abrogated the ability to inhibit p56lck kinase activity and TCR-dependent signal transduction. Incubation with thiols such as β-ME or DTT also blocked the ability of the isothiazolone to inhibit p56lck kinase activity. LC/MS anal. established the covalent modification of p56lck at cysteine residues 378, 465, and 476. Together these data support an inhibitory mechanism, whereby cysteine -SH groups within the p56lck catalytic domain react with the isothiazolone ring, leading to ring

opening and disulfide bond formation with the p56lck enzyme. Loss of p56lck activity due to -SH oxidation has been suggested to play a role in the pathol. of AIDS. Consequently, a similar mechanism of sulfhydryl oxidation leading to p56lck inhibition, described in this report, may occur in the intact T cell and may underlie certain T cell pathologies. (c) 1999 Academic Press.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ✓ ANSWER 25 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:529746 CAPLUS

TITLE: Inhibition of p56lck tyrosine kinase by methyl 3-(n-isothiazolone)-2-thiophenecarboxylate: Structure activity relationship and mechanism of action studies.

AUTHOR(S): Tu, Noah P.; Madar, David J.; BaMaung, Nwe Y.; Zhou, Xun; Wiedeman, Paul E.; Sheets, Michael P.; Ballaron, Steve J.; Trevillyan, Jim M.; Mollison, Karl W.; Warrior, Usha; Faltynek, Connie R.; Donnelly, Jennifer B.; Putman, Caton B.; Carter, George W.; Luly, Jay R.; Djuric, Stevan W.

CORPORATE SOURCE: Pharmaceutical Product Division, Abbott Laboratories, Abbott Park, IL, 60064-3500, USA

SOURCE: Book of Abstracts, 216th ACS National Meeting, Boston, August 23-27 (1998), MEDI-261. American Chemical Society: Washington, D. C. CODEN: 66KYA2

DOCUMENT TYPE: Conference; Meeting Abstract

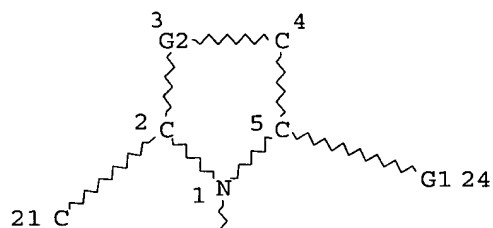
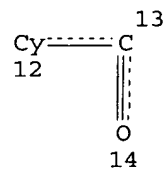
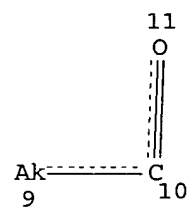
LANGUAGE: English

AB The tyrosine kinase, p56lck, is expressed predominantly in T lymphocytes and is required for T cell receptor tyrosine phosphorylation. This phosphorylation in turn leads to T cell activation and proliferation. A deficiency of p56lck leads to impairment in the activation of T cells. Accordingly, an inhibitor of this key enzyme would supply a novel immunosuppressant, potentially useful for the treatment of autoimmune diseases and transplantation rejection. High throughput screening identified the isothiazolone, 1 as a potent and selective inhibitor of this T cell kinase (IC₅₀=7μM). Structure activity studies will be described which determine the key pharmacophore of this structural class and suggest the mechanism of action.

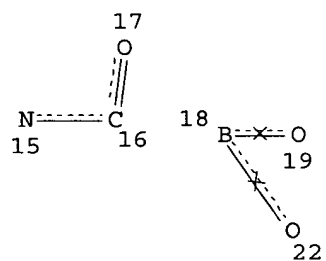
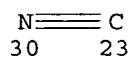
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L37 STR

31 C M2

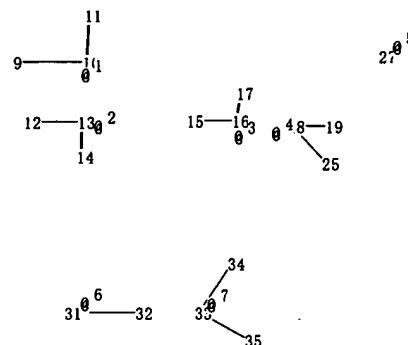
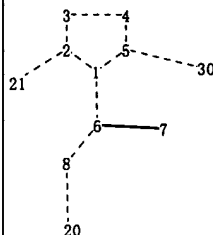
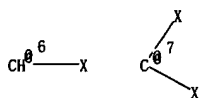
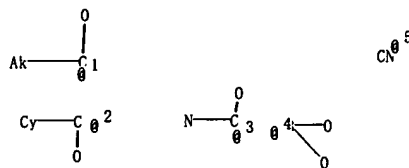
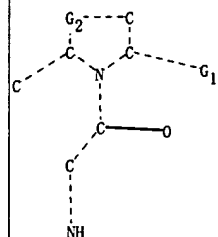


Page 1-A



28

Page 1-B



chain nodes :

6 7 9 10 11 12 13 14 15 16 17 27 30 31 32 33 34 35

ring nodes :

1 2 3 4 5

ring/chain nodes :

8 18 19 20 21 25

chain bonds :

1-6 2-21 5-30 6-7 6-8 9-10 10-11 12-13 13-14 15-16 16-17 31-32
33-34 33-35

ring/chain bonds :

8-20 18-19 18-25

ring bonds :

1-2 1-5 2-3 3-4 4-5

exact/norm bonds :

1-2 1-5 1-6 2-3 2-21 3-4 4-5 5-30 6-7 6-8 8-20 9-10 10-11
12-13 13-14 15-16 16-17 18-19 18-25 31-32 33-34 33-35

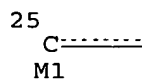
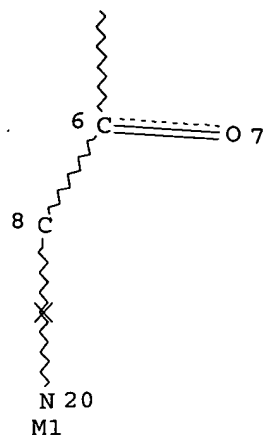
G1:[*1],[*2],[*3],[*4],[*5]

G2:CH2,[*6],[*7]

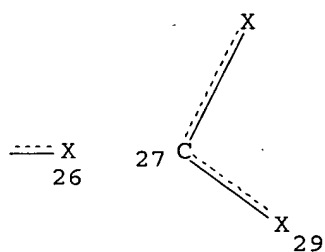
Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
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17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS 25:CLASS 27:CLASS
30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS

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Page 2-A



Page 2-B

VAR G1=10/13/16/18/23

VAR G2=31/25-2 25-4/27-2 27-4

NODE ATTRIBUTES:

| | | | | |
|--------|----|----|----|----|
| HCOUNT | IS | M1 | AT | 20 |
| HCOUNT | IS | M1 | AT | 25 |
| HCOUNT | IS | M2 | AT | 31 |
| NSPEC | IS | R | AT | 1 |
| NSPEC | IS | R | AT | 2 |
| NSPEC | IS | R | AT | 3 |
| NSPEC | IS | R | AT | 4 |
| NSPEC | IS | R | AT | 5 |
| NSPEC | IS | C | AT | 6 |
| NSPEC | IS | C | AT | 7 |
| NSPEC | IS | RC | AT | 8 |
| NSPEC | IS | C | AT | 9 |
| NSPEC | IS | C | AT | 10 |
| NSPEC | IS | C | AT | 11 |
| NSPEC | IS | C | AT | 12 |
| NSPEC | IS | C | AT | 13 |
| NSPEC | IS | C | AT | 14 |
| NSPEC | IS | C | AT | 15 |
| NSPEC | IS | C | AT | 16 |
| NSPEC | IS | C | AT | 17 |
| NSPEC | IS | RC | AT | 18 |
| NSPEC | IS | RC | AT | 19 |
| NSPEC | IS | RC | AT | 20 |
| NSPEC | IS | RC | AT | 21 |
| NSPEC | IS | RC | AT | 22 |
| NSPEC | IS | C | AT | 23 |

NSPEC IS C AT 24
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 NSPEC IS C AT 26
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 NSPEC IS C AT 29
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 DEFAULT MLEVEL IS ATOM
 MLEVEL IS CLASS AT 6 7 8 9 10 11 13 14 15 16 17 18 19 20 21 22 23
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 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 31

STEREO ATTRIBUTES: NONE

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 L41 21 SEA FILE=CAPLUS ABB=ON PLU=ON L40 NOT (PY>2002 OR AY>2002 OR
 PRY>2002)
 L43 207996 SEA FILE=CAPLUS ABB=ON PLU=ON (DIABET?/OBI OR ANTI/OBI(2A)DIA
 BETE?/OBI OR INSULIN?/OBI)
 L44 256730 SEA FILE=CAPLUS ABB=ON PLU=ON (DIABET? OR ANTI(2A)DIABETE?
 OR INSULIN?)/BI
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 L46 23630 SEA FILE=CAPLUS ABB=ON PLU=ON ANTIDIABET?/BI,OBI
 L47 6 SEA FILE=CAPLUS ABB=ON PLU=ON L46 AND L40
 L48 7 SEA FILE=CAPLUS ABB=ON PLU=ON (L47 OR L45)
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 L50 28 SEA FILE=CAPLUS ABB=ON PLU=ON L40 AND P/DT
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L51 ANSWER 1 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2006:151226 CAPLUS
 DOCUMENT NUMBER: 144:233382
 TITLE: Preparation of tetrapeptide analogs for treatment of
 hyperproliferative diseases
 INVENTOR(S): Chao, Bin; Deckwerth, Thomas L.; Furth, Paul S.;
 Linton, Steven D.; Spada, Alfred P.; Ullman, Brett R.;
 Weinhouse, Michael I.
 PATENT ASSIGNEE(S): Idun Pharmaceuticals, Inc., USA
 SOURCE: PCT Int. Appl., 316 pp., which
 CODEN: PIXXD2
 DOCUMENT TYPE: **Patent**
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2006017295 | A2 | 20060216 | WO 2005-US24700 | 20050712 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, | | | | |

NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 2004-587471P P 20040712

US 2005-683875P P 20050523

OTHER SOURCE(S): MARPAT 144:233382

AB The invention relates to compds. R5R6NCR3R4CONHCR8R9CONR10CHR7-M-NR1R2 [M is CO, SO or SO₂; R1 is H; R2 is aryl, heteroaryl, cycloalkyl, cycloalkylalkyl or heterocyclyl; R3 is H or alkyl; R4 is alkyl; R5 is H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroarylium, cycloalkyl, heterocyclyl or an amino group; or R3 or R4 may form a ring with R5; R6 is H, alkyl, alkenyl or alkynyl; R7 is H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl or heterocyclyl; R8, R9 are independently H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl or heterocyclyl; R10 is alkyl, aryl or cycloalkyl; or R10 may form a ring with R8 or R9] or a pharmaceutically-acceptable derivative, which are peptidomimetics of the N-terminal tetrapeptide of the mitochondrial protein Smac believed to promote apoptosis in cells through a pathway involving the Inhibitor of Apoptosis Proteins (IAPs). These peptidomimetics bind IAPs and are useful for the treatment of hyperproliferative diseases such as cancer. Thus, 6-(2-methylaminopropionylamino)-5-oxooctahydropyrrolo[1,2-a]azepine-3-carboxylic acid (1,2,3,4-tetrahydronaphthalen-1-yl)amide was prepared by a multistep sequence involving ring-forming metathesis and peptide coupling reactions and showed EC₅₀ < 1 μ M for relief of BIR3-mediated caspase-9 inhibition.

IT 876622-87-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of tetrapeptide analogs for treatment of hyperproliferative diseases)

RN 876622-87-6 CAPLUS

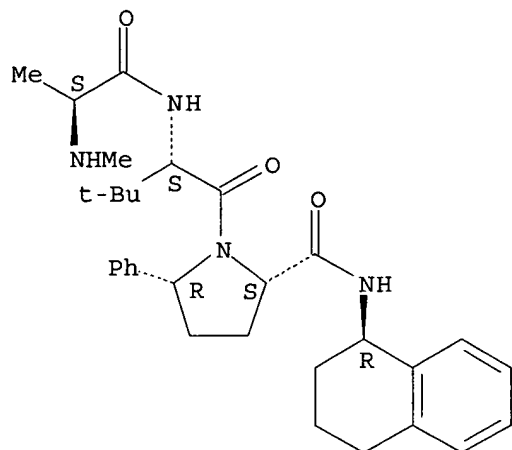
CN L-Prolinamide, N-methyl-L-alanyl-3-methyl-L-valyl-5-phenyl-N-[(1R)-1,2,3,4-tetrahydro-1-naphthalenyl]-, (5R)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

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CRN 876622-86-5

CMF C31 H42 N4 O3

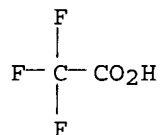
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



IT 876624-26-9P

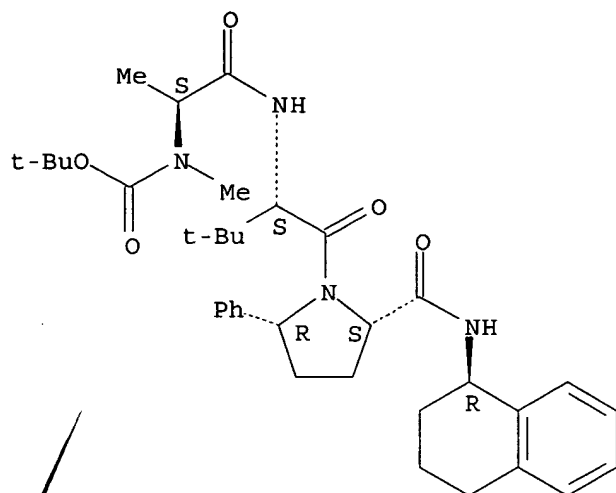
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of tetrapeptide analogs for treatment of hyperproliferative diseases)

RN 876624-26-9 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-N-methyl-L-alanyl-3-methyl-L-valyl-5-phenyl-N-[(1R)-1,2,3,4-tetrahydro-1-naphthalenyl]-, (5R)-(9CI)
(CA INDEX NAME)

Absolute stereochemistry.



✓ L51 ANSWER 2 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1103744 CAPLUS

DOCUMENT NUMBER: 143:367204

TITLE: Preparation of dicyanopyrrolidines as dipeptidyl
peptidase IV inhibitors

INVENTOR(S): McClure, Lester Dennis; Olson, Thanh Vu; Wright,
Stephen Wayne

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 51 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2005095339 | A1 | 20051013 | WO 2005-IB721 | 20050318 |
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| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

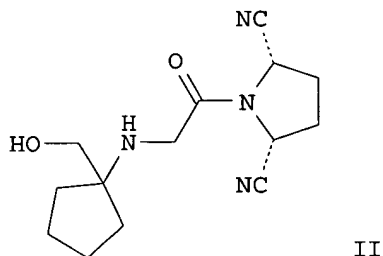
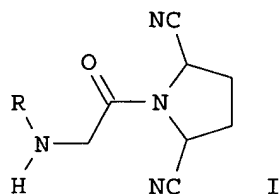
PRIORITY APPLN. INFO.:

US 2004-558472P

P 20040331

OTHER SOURCE(S): MARPAT 143:367204

GI



AB Title compds. I [R = R1-X-Y-(CH2)m- or R1-X-Y-(CH2)n(C(CH3)2)-; X = bond, O, S, etc.; Y = bond or N(R2) with provisions; R1 = (un)substituted phenylalkyl, phenoxyalkyl, heterocycloalkyl, etc.; R2 = H, alkyl or cycloalkyl; m = 2-4; n = 1-3] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of dipeptidyl peptidase IV (DDP-IV). Thus, e.g., II was prepared by acylation of cis-1-benzhydryl-pyrrolidine-2,5-dicarbonitrile (preparation given) with bromoacetyl bromide and subsequent coupling with 1-hydroxymethyl-cyclohexylamine. The inhibitory activity of I was evaluated in vitro using spectrophotometric assays (no data). I as inhibitors of DDP-IV should prove useful in the treatment of type 1 and type 2 **diabetes**, arthritis and obesity. Pharmaceutical compns. comprising I are disclosed.

IT 813433-92-0P 866396-28-3P 866396-29-4P
 866396-30-7P 866396-31-8P 866396-32-9P
 866396-33-0P 866396-34-1P 866396-35-2P
 866396-36-3P 866396-37-4P 866396-38-5P
 866396-39-6P 866396-40-9P 866396-41-0P
 866396-42-1P 866396-43-2P 866396-44-3P
 866396-45-4P 866396-46-5P 866396-47-6P
 866396-48-7P 866396-49-8P 866396-50-1P
 866396-51-2P 866396-52-3P 866396-53-4P
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 866396-63-6P 866396-64-7P 866396-65-8P
 866396-66-9P 866396-67-0P 866396-68-1P
 866396-69-2P 866396-70-5P 866453-66-9P
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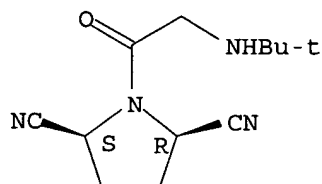
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of dicyanopyrrolidines as dipeptidyl peptidase IV inhibitors)

RN 813433-92-0 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[(1,1-dimethylethyl)amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

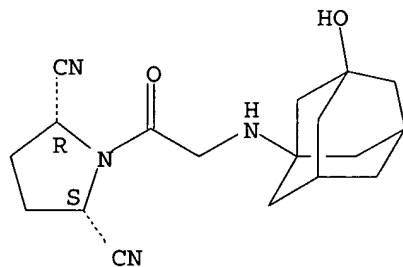
Relative stereochemistry.



RN 866396-28-3 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[(3-hydroxytricyclo[3.3.1.1^{3,7}]dec-1-yl)amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

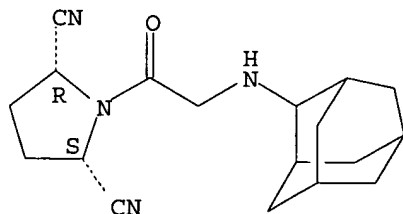
Relative stereochemistry.



RN 866396-29-4 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[(tricyclo[3.3.1.1^{3,7}]dec-2-yl)amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

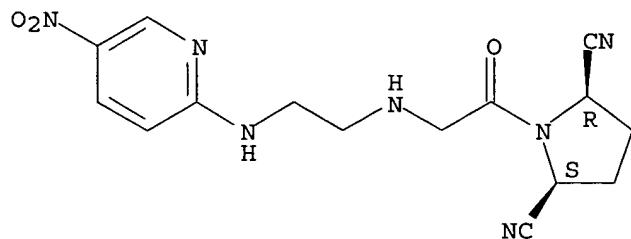
Relative stereochemistry.



RN 866396-30-7 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[2-[(5-nitro-2-pyridinyl)amino]ethyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

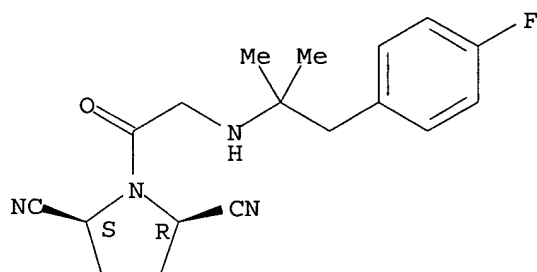
Relative stereochemistry.



RN 866396-31-8 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[2-(4-fluorophenyl)-1,1-dimethylethyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

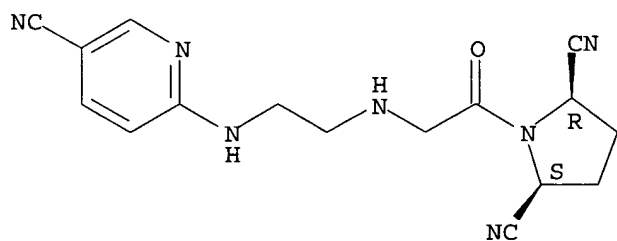
Relative stereochemistry.



RN 866396-32-9 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[2-[(5-cyano-2-pyridinyl)amino]ethyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

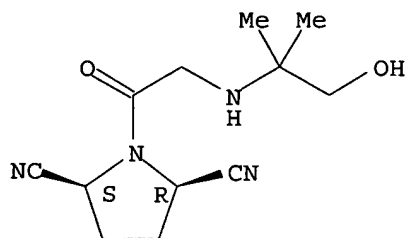
Relative stereochemistry.



RN 866396-33-0 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[2-(2-hydroxy-1,1-dimethylethyl)amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

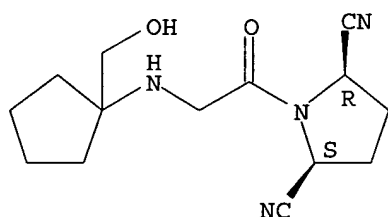
Relative stereochemistry.



RN 866396-34-1 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-(hydroxymethyl)cyclopentyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

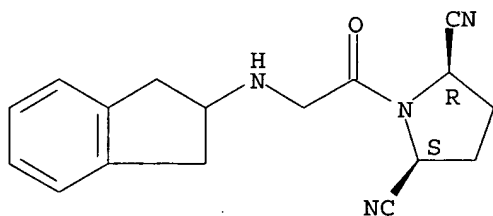
Relative stereochemistry.



RN 866396-35-2 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[2,3-dihydro-1H-inden-2-yl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

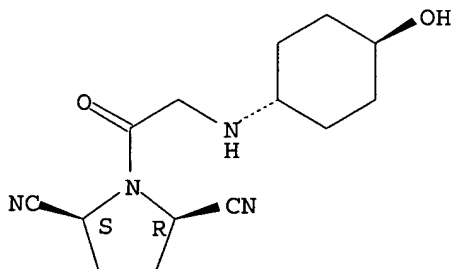
Relative stereochemistry.



RN 866396-36-3 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[trans-4-hydroxycyclohexyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

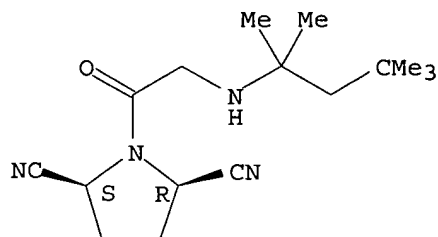
Relative stereochemistry.



RN 866396-37-4 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[(1,1,3,3-tetramethylbutyl)amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

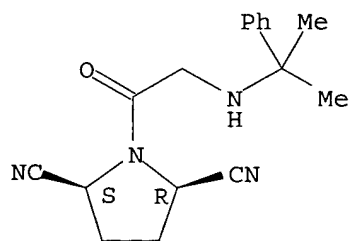
Relative stereochemistry.



RN 866396-38-5 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[(1-methyl-1-phenylethyl)amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

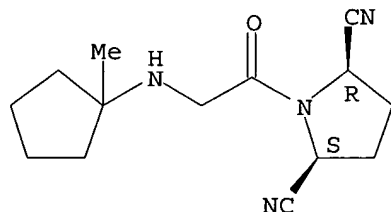
Relative stereochemistry.



RN 866396-39-6 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[(1-methylcyclopentyl)amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

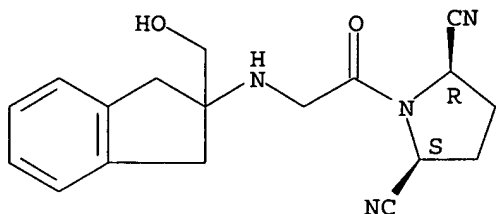
Relative stereochemistry.



RN 866396-40-9 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[2,3-dihydro-2-(hydroxymethyl)-1H-inden-2-yl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

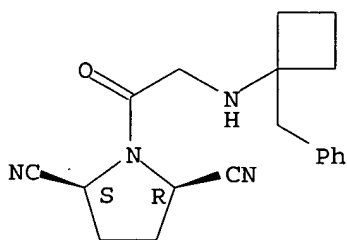
Relative stereochemistry.



RN 866396-41-0 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-(phenylmethyl)cyclobutyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

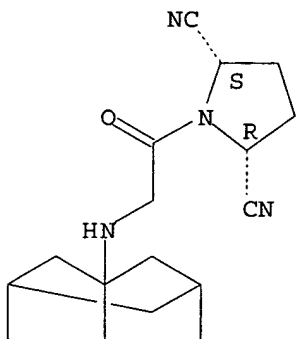
Relative stereochemistry.



RN 866396-42-1 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-(hexahydro-2,5-methanopentalen-3a(1H)-yl)amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

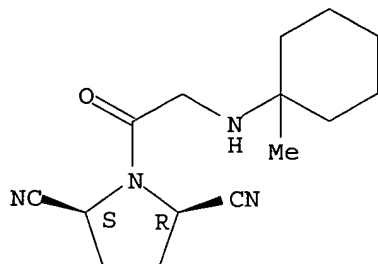
Relative stereochemistry.



RN 866396-43-2 CAPLUS

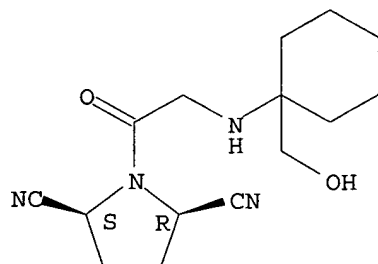
CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-(1-methylcyclohexyl)amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



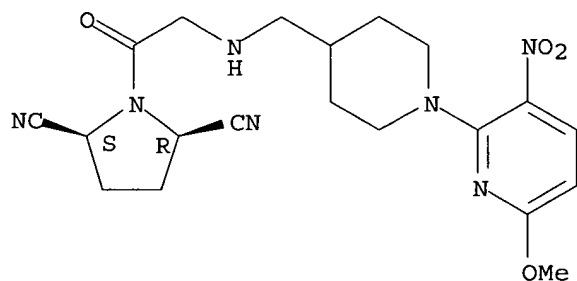
RN 866396-44-3 CAPLUS
 CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-(hydroxymethyl)cyclohexyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



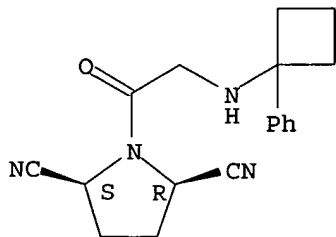
RN 866396-45-4 CAPLUS
 CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-(6-methoxy-3-nitro-2-pyridinyl)-4-piperidinyl]methyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 866396-46-5 CAPLUS
 CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-(phenylcyclobutyl)amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

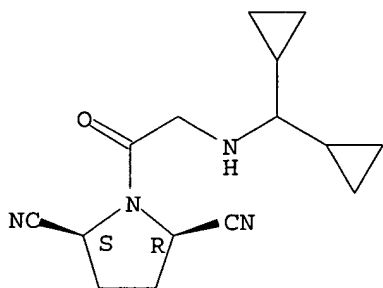
Relative stereochemistry.



RN 866396-47-6 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[dicyclopropylmethyl)amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

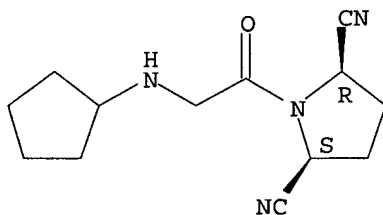
Relative stereochemistry.



RN 866396-48-7 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[(cyclopentylamino)acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

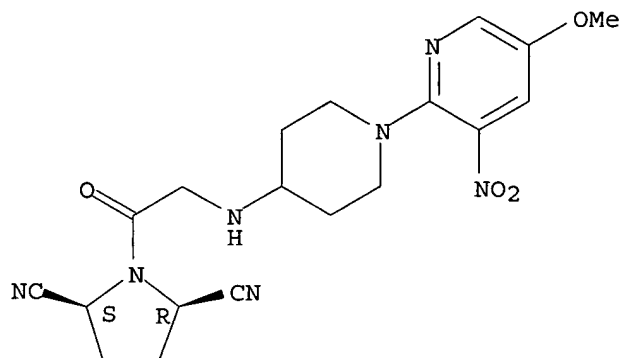
Relative stereochemistry.



RN 866396-49-8 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-(5-methoxy-3-nitro-2-pyridinyl)-4-piperidinyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

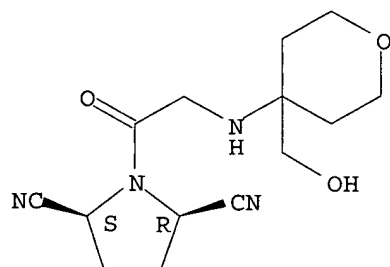
Relative stereochemistry.



RN 866396-50-1 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[tetrahydro-4-(hydroxymethyl)-2H-pyran-4-yl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

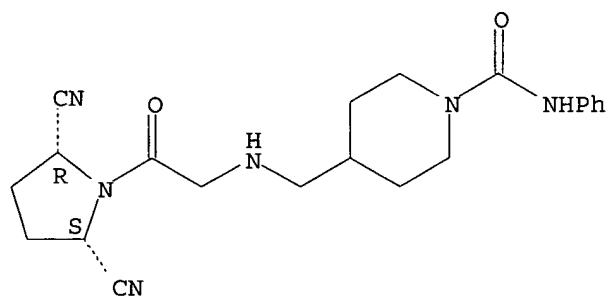
Relative stereochemistry.



RN 866396-51-2 CAPLUS

CN 1-Piperidinecarboxamide, 4-[[[2-[(2R,5S)-2,5-dicyano-1-pyrrolidinyl]-2-oxoethyl]amino]methyl]-N-phenyl-, rel- (9CI) (CA INDEX NAME)

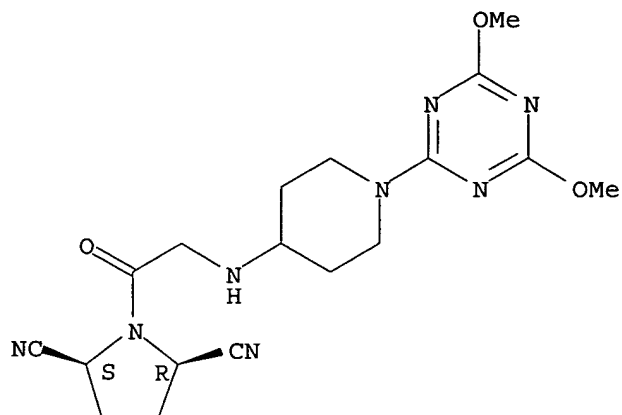
Relative stereochemistry.



RN 866396-52-3 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-piperidinyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

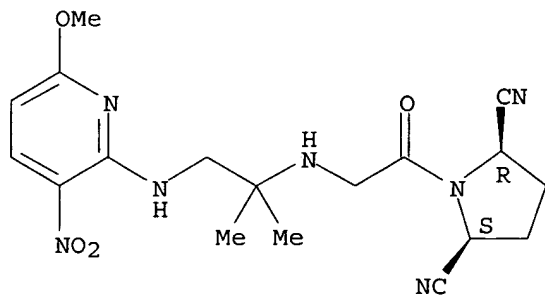
Relative stereochemistry.



RN 866396-53-4 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[2-[(6-methoxy-3-nitro-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

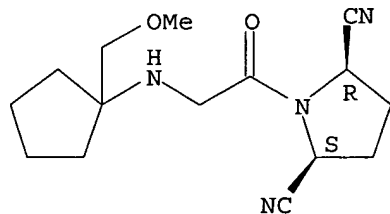
Relative stereochemistry.



RN 866396-54-5 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-(methoxymethyl)cyclopentyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

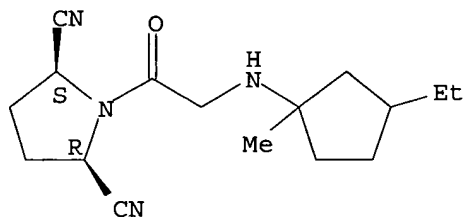
Relative stereochemistry.



RN 866396-55-6 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[3-ethyl-1-methylcyclopentyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

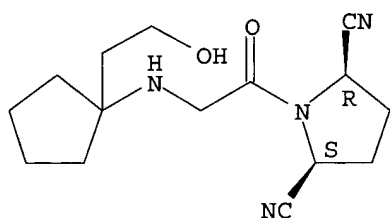
Relative stereochemistry.



RN 866396-56-7 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-(2-hydroxyethyl)cyclopentyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

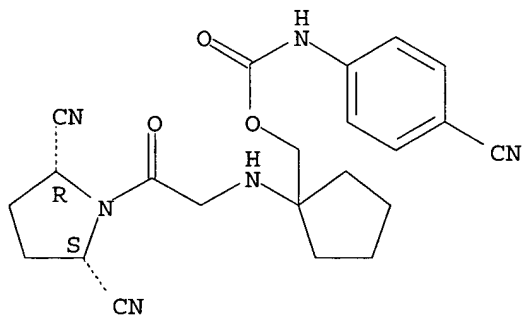
Relative stereochemistry.



RN 866396-57-8 CAPLUS

CN Carbamic acid, (4-cyanophenyl)-, [1-[[2-[(2R,5S)-2,5-dicyano-1-pyrrolidinyl]-2-oxoethyl]amino]cyclopentyl]methyl ester, rel- (9CI) (CA INDEX NAME)

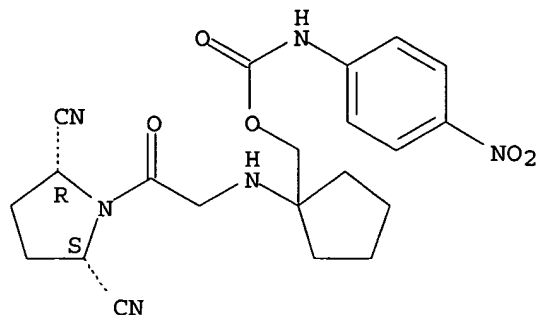
Relative stereochemistry.



RN 866396-58-9 CAPLUS

CN Carbamic acid, (4-nitrophenyl)-, [1-[[2-[(2R,5S)-2,5-dicyano-1-pyrrolidinyl]-2-oxoethyl]amino]cyclopentyl]methyl ester, rel- (9CI) (CA INDEX NAME)

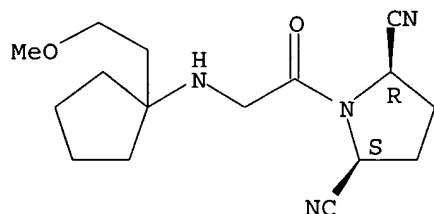
Relative stereochemistry.



RN 866396-59-0 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-(2-methoxyethyl)cyclopentyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

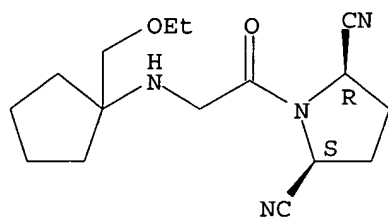
Relative stereochemistry.



RN 866396-60-3 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-(ethoxymethyl)cyclopentyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

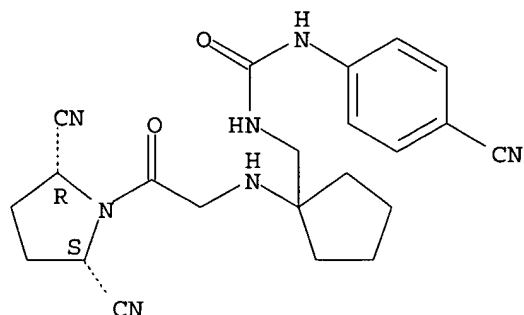
Relative stereochemistry.



RN 866396-61-4 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-[[[(4-cyanophenyl)amino]carbonyl]amino]methyl]cyclopentyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

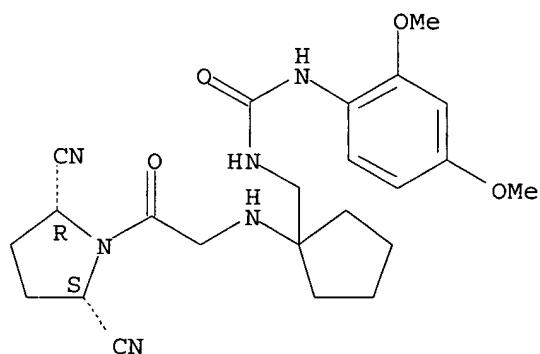
Relative stereochemistry.



RN 866396-62-5 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-[[[(2,4-dimethoxyphenyl)amino]carbonyl]amino]methyl]cyclopentyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

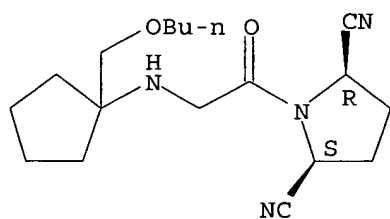
Relative stereochemistry.



RN 866396-63-6 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-(butoxymethyl)cyclopentyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

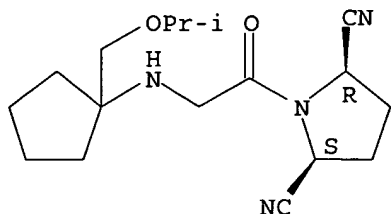
Relative stereochemistry.



RN 866396-64-7 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-[(1-methylethoxy)methyl]cyclopentyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

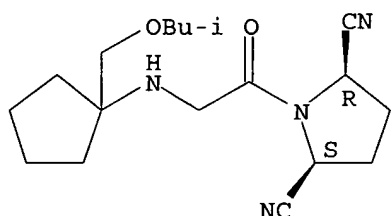
Relative stereochemistry.



RN 866396-65-8 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-[(2-methylpropoxy)methyl]cyclopentyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

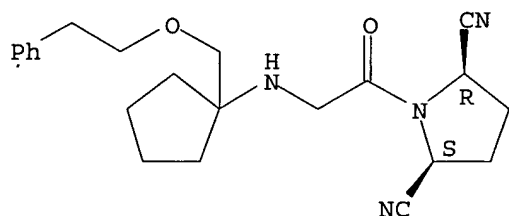
Relative stereochemistry.



RN 866396-66-9 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-[(2-phenylethoxy)methyl]cyclopentyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

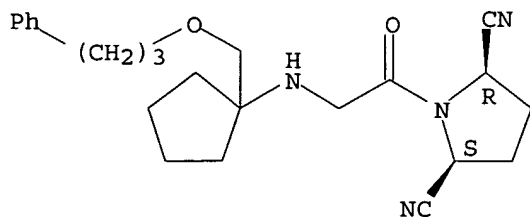
Relative stereochemistry.



RN 866396-67-0 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-[(3-phenylpropoxy)methyl]cyclopentyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

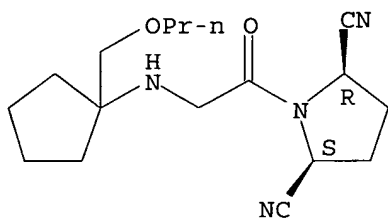
Relative stereochemistry.



RN 866396-68-1 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-(propoxymethyl)cyclopentyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

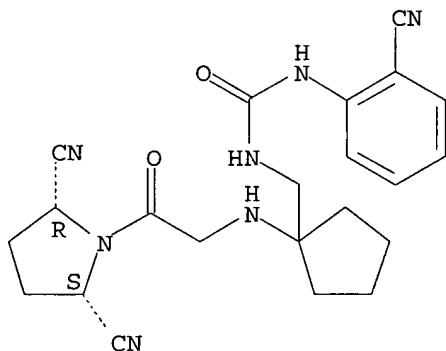
Relative stereochemistry.



RN 866396-69-2 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-[[[(2-cyanophenyl)amino]carbonyl]amino]methyl]cyclopentyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

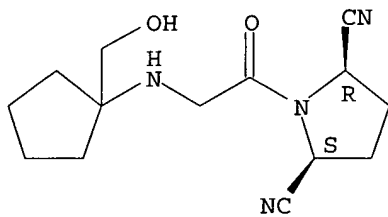
Relative stereochemistry.



RN 866396-70-5 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-(hydroxymethyl)cyclopentyl]amino]acetyl]-, monohydrochloride, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

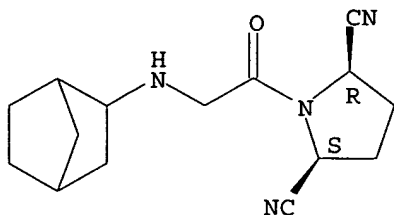


● HCl

RN 866453-66-9 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[(bicyclo[2.2.1]hept-2-ylamino)acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

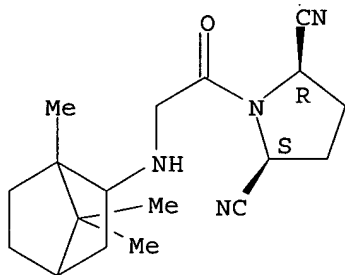
Relative stereochemistry.



RN 866453-67-0 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[(1,7,7-trimethylbicyclo[2.2.1]hept-2-yl)amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

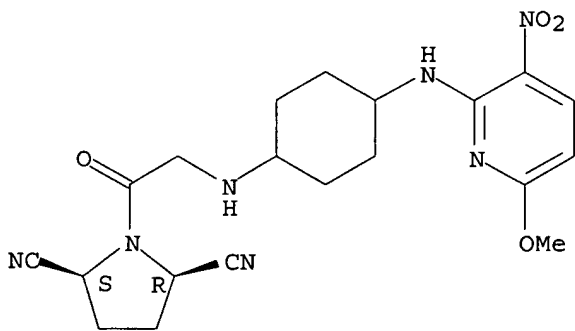
Relative stereochemistry.



RN 866453-68-1 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[4-[(6-methoxy-3-nitro-2-pyridinyl)amino]cyclohexyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

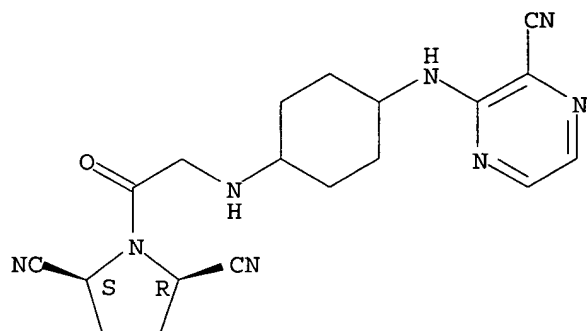
Relative stereochemistry.



RN 866453-69-2 CAPLUS

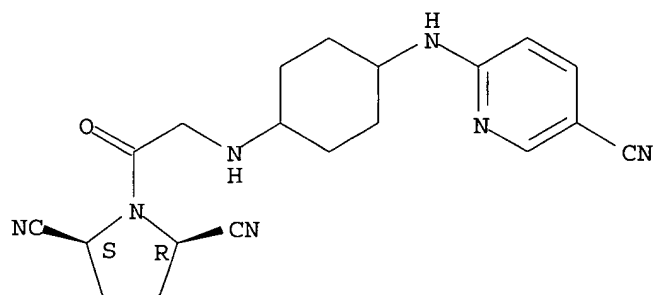
CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[4-[(3-cyanopyrazinyl)amino]cyclohexyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



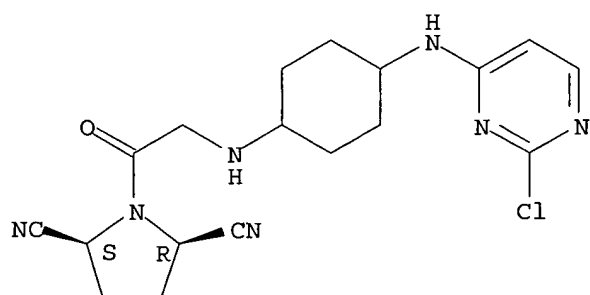
RN 866453-70-5 CAPLUS
 CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[4-[(5-cyano-2-pyridinyl)amino]cyclohexyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



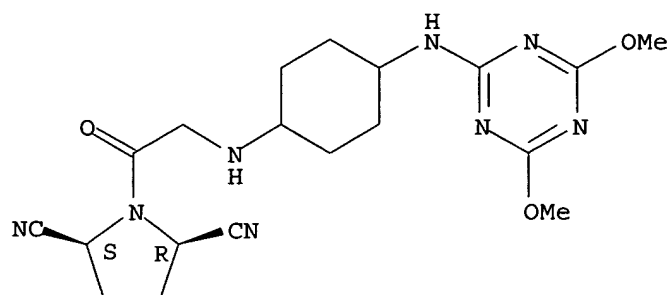
RN 866453-71-6 CAPLUS
 CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[4-[(2-chloro-4-pyrimidinyl)amino]cyclohexyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 866453-72-7 CAPLUS
 CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[4-[(4,6-dimethoxy-1,3,5-triazin-2-yl)amino]cyclohexyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

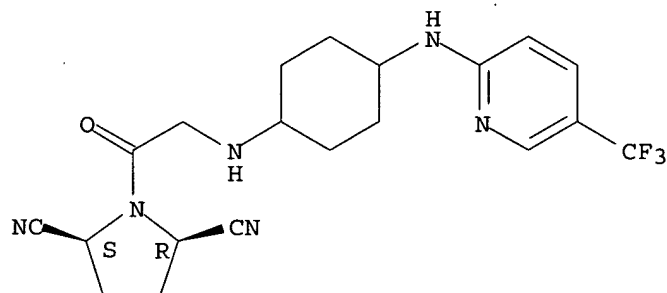
Relative stereochemistry.



RN 866453-73-8 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[4-[[5-(trifluoromethyl)-2-pyridinyl]amino]cyclohexyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

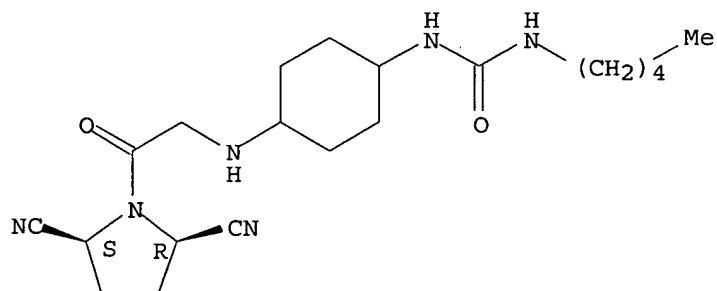
Relative stereochemistry.



RN 866453-74-9 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[4-[[5-(trifluoromethyl)-2-pyridinyl]amino]cyclohexyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

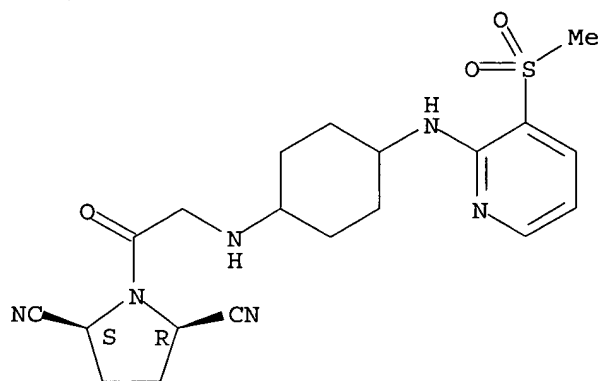
Relative stereochemistry.



RN 866453-75-0 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[4-[[5-(trifluoromethyl)-2-pyridinyl]amino]cyclohexyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

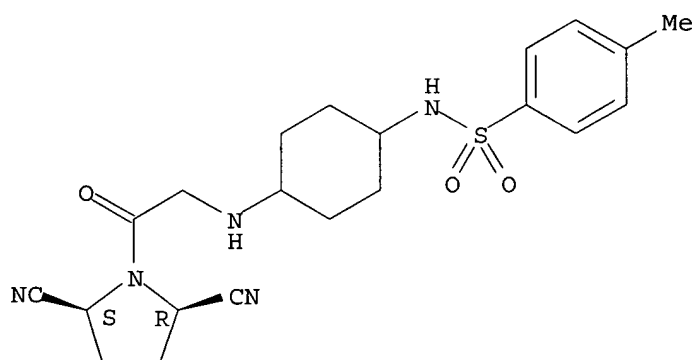
Relative stereochemistry.



RN 866453-76-1 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[4-[(4-methylphenyl)sulfonyl]amino]cyclohexyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

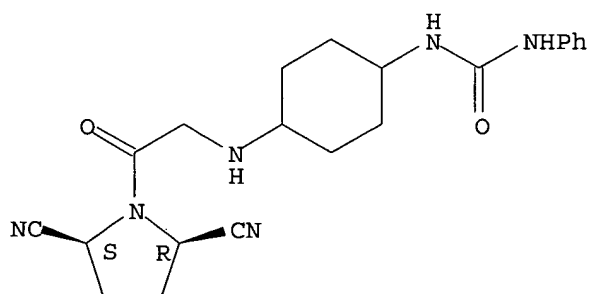
Relative stereochemistry.



RN 866453-77-2 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[4-[(phenylamino)carbonyl]amino]cyclohexyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

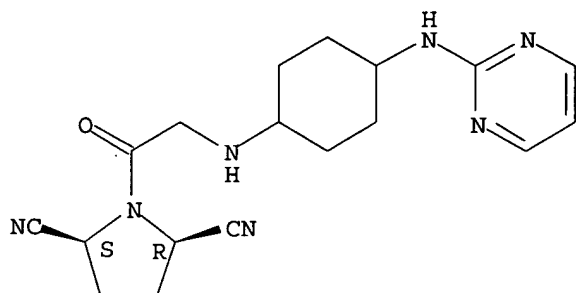


RN 866453-78-3 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[4-(2-pyrimidinylamino)cyclohexyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

lacetlyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

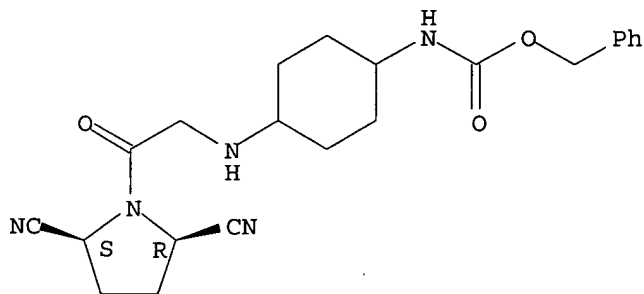
Relative stereochemistry.



RN 866453-79-4 CAPLUS

CN Carbamic acid, [4-[[2-[(2R,5S)-2,5-dicyano-1-pyrrolidinyl]-2-oxoethyl]amino]cyclohexyl]-, phenylmethyl ester, rel- (9CI) (CA INDEX NAME)

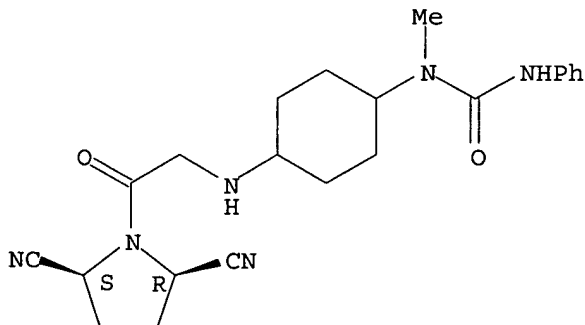
Relative stereochemistry.



RN 866453-80-7 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[4-[methyl[(phenylamino)carbonyl]amino]cyclohexyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

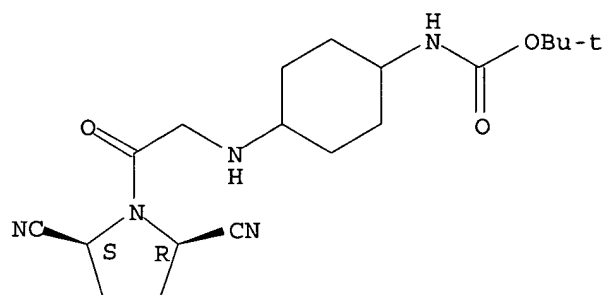


RN 866453-81-8 CAPLUS

CN Carbamic acid, [4-[[2-[(2R,5S)-2,5-dicyano-1-pyrrolidinyl]-2-

oxoethyl]amino]cyclohexyl]-, 1,1-dimethylethyl ester, rel- (9CI) (CA
INDEX NAME)

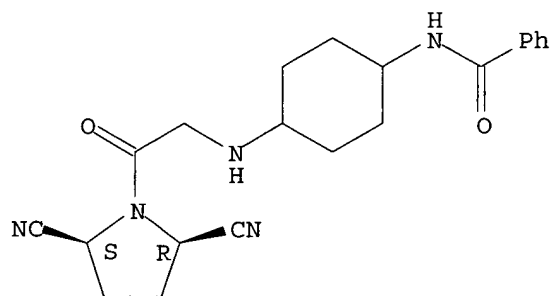
Relative stereochemistry.



RN 866453-82-9 CAPLUS

CN Benzamide, N-[4-[[2-[(2R,5S)-2,5-dicyano-1-pyrrolidinyl]-2-oxoethyl]amino]cyclohexyl]-, rel- (9CI) (CA INDEX NAME)

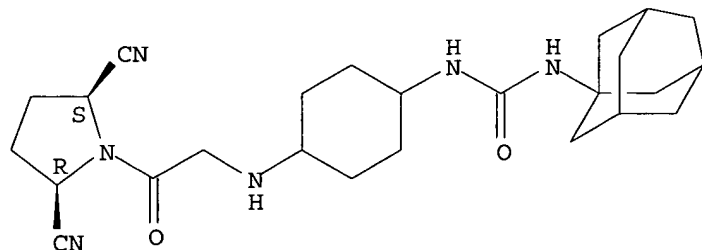
Relative stereochemistry.



RN 866453-83-0 CAPLUS

| | | |
|----|---|-----|
| CN | 2,5-Pyrrolidinedicarbonitrile, 1-[[[4-[[[(tricyclo[3.3.1.1 ^{3,7}]dec-1-ylamino)carbonyl]amino]cyclohexyl]amino]acetyl]-, (2R,5S)-rel- (9CI) | (CA |
| | INDEX NAME) | |

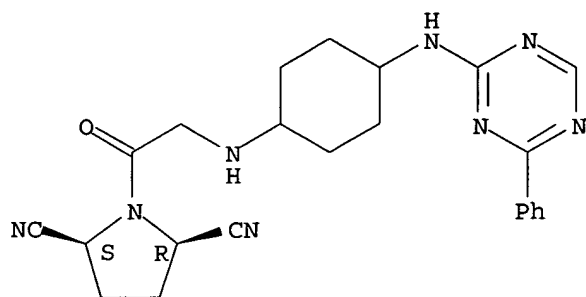
Relative stereochemistry.



RN 866453-84-1 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[4-[(4-phenyl-1,3,5-triazin-2-yl)amino]cyclohexyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

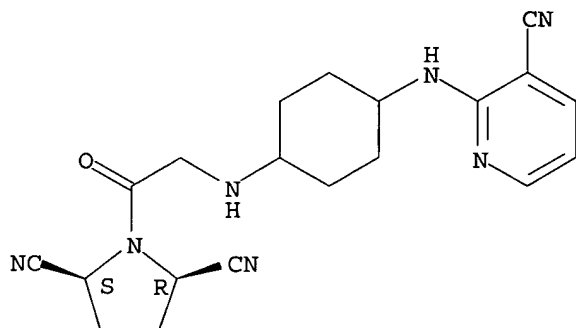
Relative stereochemistry.



RN 866453-85-2 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[4-[(3-cyano-2-pyridinyl)amino]cyclohexyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

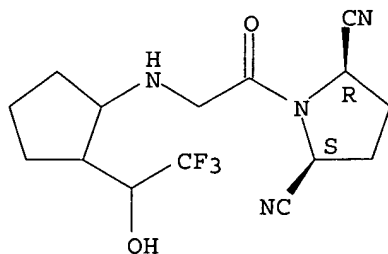
Relative stereochemistry.



RN 866453-86-3 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[2-(2,2,2-trifluoro-1-hydroxyethyl)cyclopentyl]amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

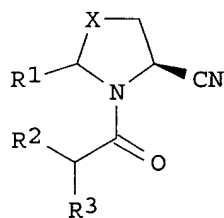
L51 ANSWER 3 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1050935 CAPLUS

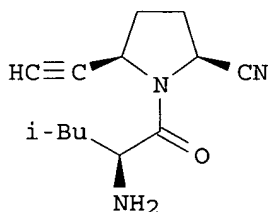
DOCUMENT NUMBER: 143:347048
 TITLE: Preparation of cyanopyrrolidine derivatives and pharmaceutical compositions thereof as inhibitors of dipeptidyl peptidase-iv (dpp-iv)
 INVENTOR(S): Madar, David J.; Djuric, Stevan W.; Michmerhuizen, Melissa J.; Kopecka, Hana A.; Li, Xiaofeng; Longenecker, Kenton L.; Pei, Zhonghua; Pireh, Daisy; Sham, Hing L.; Stewart, Kent D.; Szczepankiewicz, Bruce G.; Wiedeman, Paul E.; Yong, Hong
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 70 pp., Cont.-in-part of U.S. Ser. No. 788,993.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|------------------------|
| US 2005215784 | A1 | 20050929 | US 2005-36258 | 20050113 |
| US 2004121964 | A1 | 20040624 | US 2003-659860 | 20030911 |
| US 2004259843 | A1 | 20041223 | US 2004-788993 | 20040227 |
| PRIORITY APPLN. INFO.: | | | US 2002-412084P | P 20020919 |
| | | | US 2003-659860 | A2 20030911 |
| | | | US 2004-788993 | A2 20040227 |

OTHER SOURCE(S): MARPAT 143:347048
 GI



I



II

AB Title compds. I [R1 = alkynyl or cyano; R2 and R3 independently = H, alkyl, alkenyl etc.; or R2 and R3 together form (un)substituted heterocycle; X = CH₂, CHF, CF₂], and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of dipeptidyl peptidase IV (DPP-IV). Thus, e.g., II·HCl was prepared in a multistep synthesis from Me (S)-(+)-2-pyrrolidone-5-carboxylate. K_i values for DPP-IV assays of selected compds. ranged from 1-130 nM. And are useful for the prevention or treatment of **diabetes**, especially type II **diabetes**, as well as hyperglycemia, Syndrome X, hyperinsulinemia, obesity, atherosclerosis, and various immunomodulatory diseases.

IT 676561-27-6P 676562-23-5P 865980-28-5P

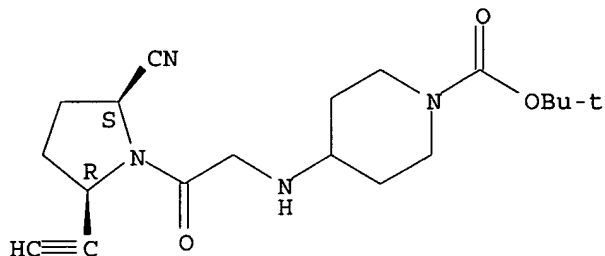
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of cyanopyrrolidine derivs. and pharmaceutical compns. thereof as inhibitors of dipeptidyl peptidase-iv (dpp-iv))

RN 676561-27-6 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

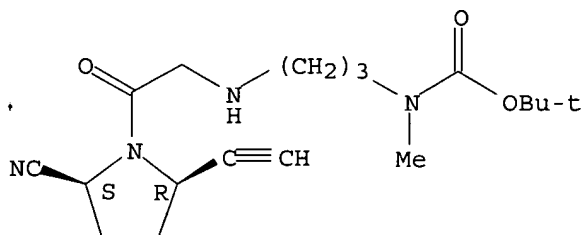
Absolute stereochemistry.



RN 676562-23-5 CAPLUS

CN Carbamic acid, [3-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]propyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

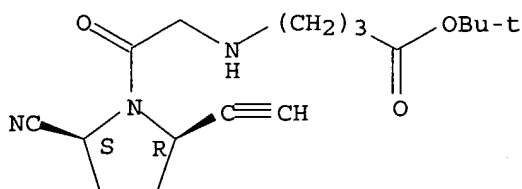
Absolute stereochemistry.



RN 865980-28-5 CAPLUS

CN Butanoic acid, 4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 676559-41-4P 676559-47-0P 676559-48-1P
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 676559-64-1P 676559-65-2P 676559-70-9P
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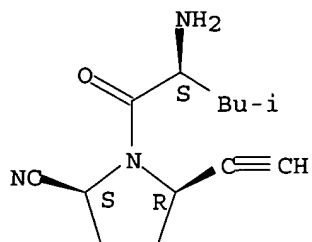
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of cyanopyrrolidine derivs. and pharmaceutical compns. thereof
 as inhibitors of dipeptidyl peptidase-iv (dpp-iv))

RN 676559-41-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-5-ethynyl-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

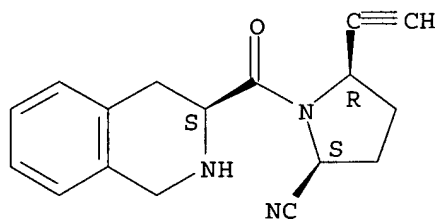


● HCl

RN 676559-47-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(3S)-1,2,3,4-tetrahydro-3-isoquinolinyl]carbonyl]-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

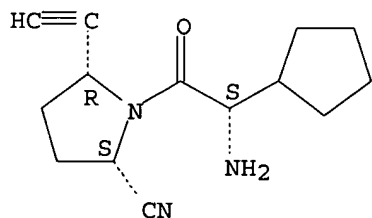


● HCl

RN 676559-48-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclopentylacetyl]-5-ethynyl-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

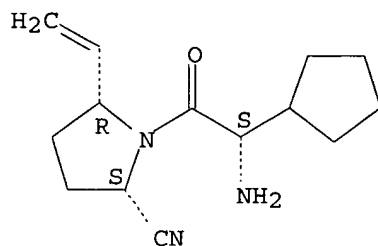


● HCl

RN 676559-54-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclopentylacetyl]-5-ethenyl-,
monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

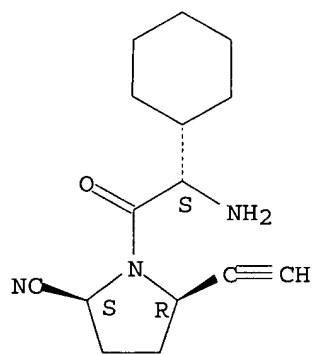


● HCl

RN 676559-56-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclohexylacetyl]-5-ethynyl-,
monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

RN 676559-58-3 CAPLUS

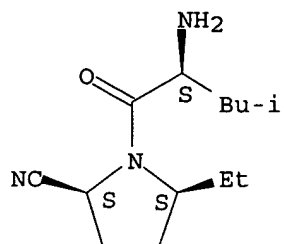
CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-5-ethyl-,
(2S,5S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 676559-57-2

CMF C13 H23 N3 O

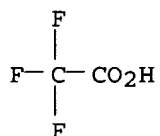
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 676559-64-1 CAPLUS

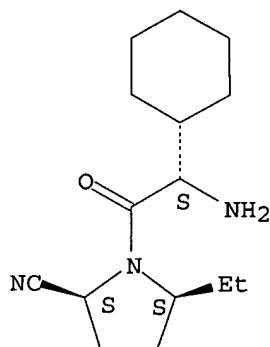
CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclohexylacetyl]-5-ethyl-, (2S,5S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 676559-63-0

CMF C15 H25 N3 O

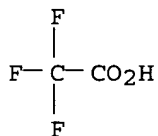
Absolute stereochemistry.



CM 2

CRN 76-05-1

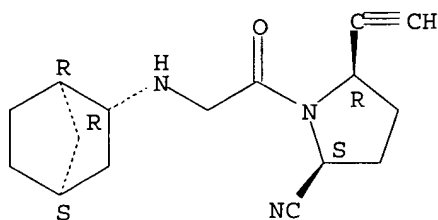
CMF C2 H F3 O2



RN 676559-65-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(1R,2R,4S)-bicyclo[2.2.1]hept-2-ylamino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

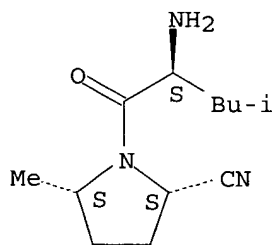
Absolute stereochemistry.



RN 676559-70-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

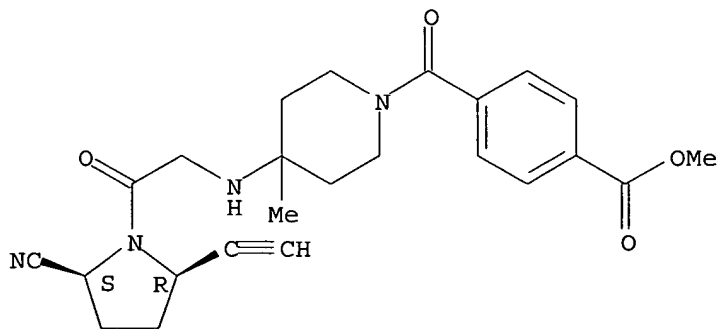
Absolute stereochemistry.



RN 676559-80-1 CAPLUS

CN Benzoic acid, 4-[[4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-4-methyl-1-piperidinyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

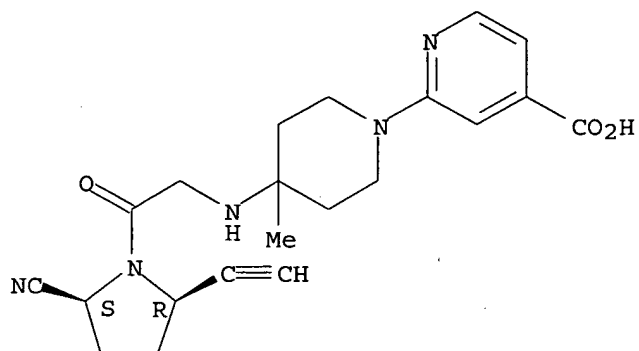
Absolute stereochemistry.



RN 676559-83-4 CAPLUS

CN 4-Pyridinecarboxylic acid, 2-[4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-4-methyl-1-piperidinyl]- (9CI) (CA INDEX NAME)

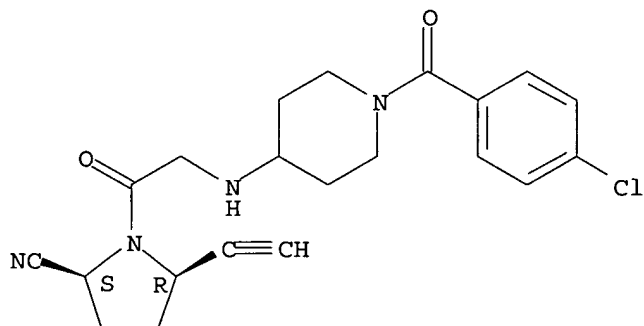
Absolute stereochemistry.



RN 676559-86-7 CAPLUS

CN 4-Piperidinamine, 1-(4-chlorobenzoyl)-N-[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

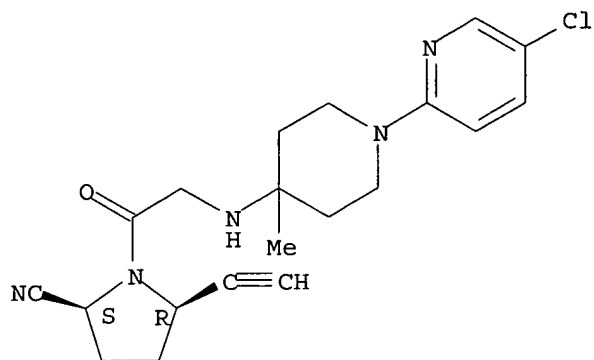
Absolute stereochemistry.



RN 676559-88-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-chloro-2-pyridinyl)-4-methyl-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

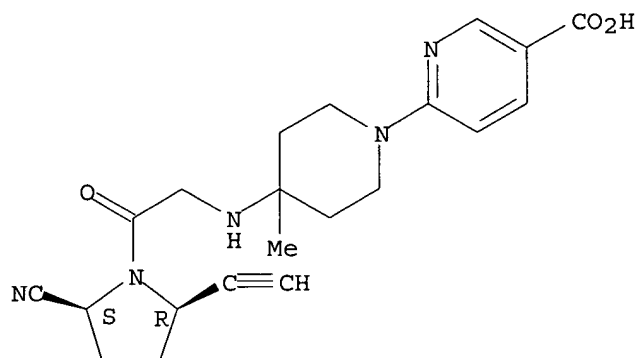
Absolute stereochemistry.



RN 676559-99-2 CAPLUS

CN 3-Pyridinecarboxylic acid, 6-[4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-4-methyl-1-piperidinyl]- (9CI) (CA INDEX NAME)

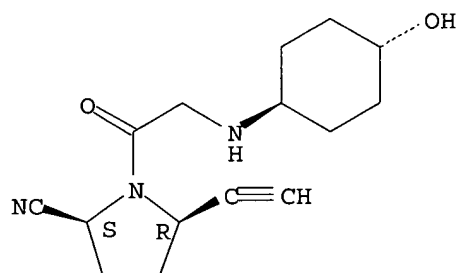
Absolute stereochemistry.



RN 676560-07-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-hydroxycyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

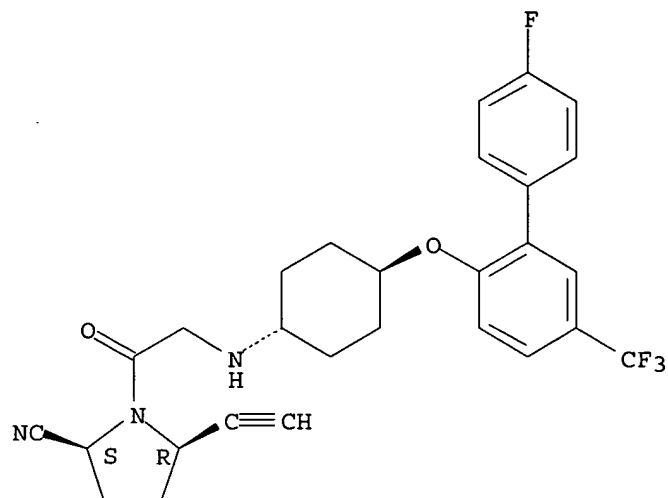
Absolute stereochemistry.



RN 676560-08-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[4'-fluoro-5-(trifluoromethyl)[1,1'-biphenyl]-2-yl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

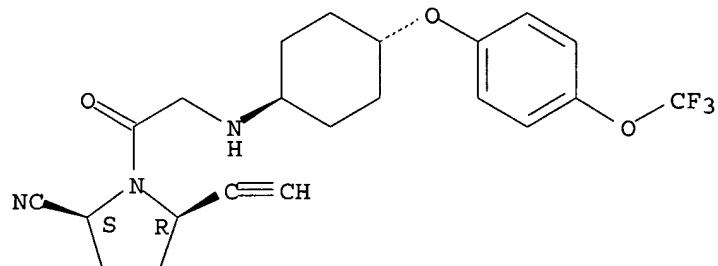
Absolute stereochemistry.



RN 676560-13-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[4-(trifluoromethoxy)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

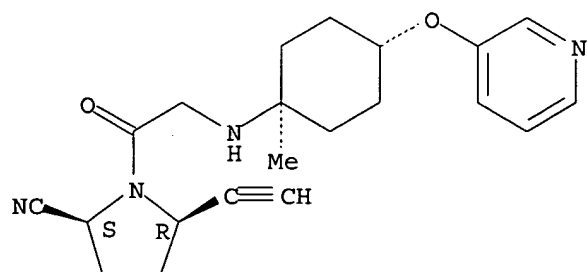
Absolute stereochemistry.



RN 676560-22-8 CAPLUS

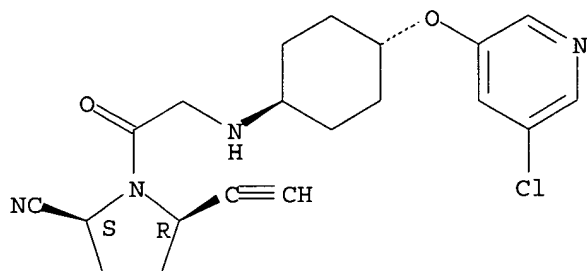
CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-1-methyl-4-(3-pyridinyloxy)cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



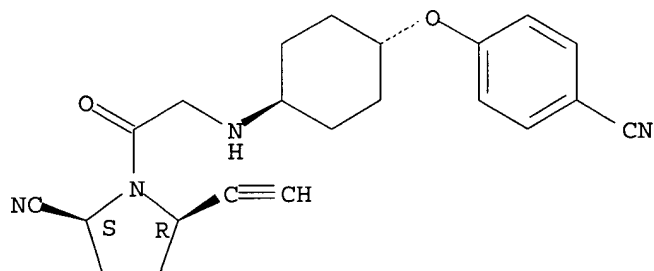
RN 676560-23-9 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(5-chloro-3-pyridinyl)oxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



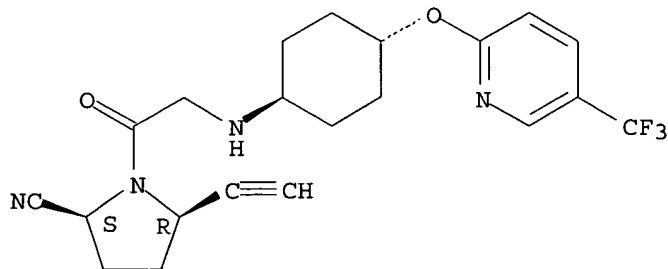
RN 676560-25-1 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(4-cyanophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



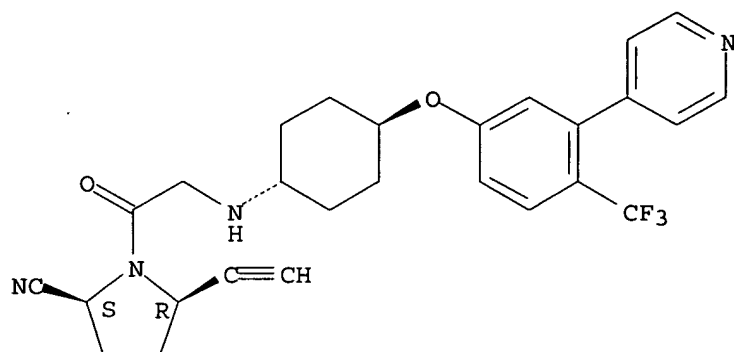
RN 676560-27-3 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[5-(trifluoromethyl)-2-pyridinyl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676560-29-5 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[3-(4-pyridinyl)-4-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

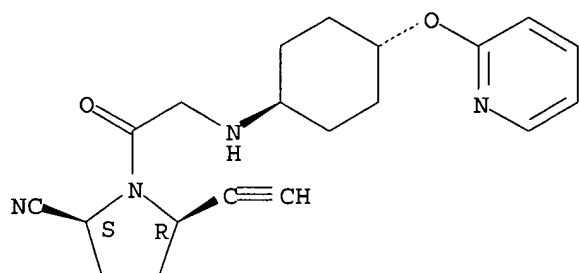
Absolute stereochemistry.



RN 676560-34-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-(2-pyridinyloxy)cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

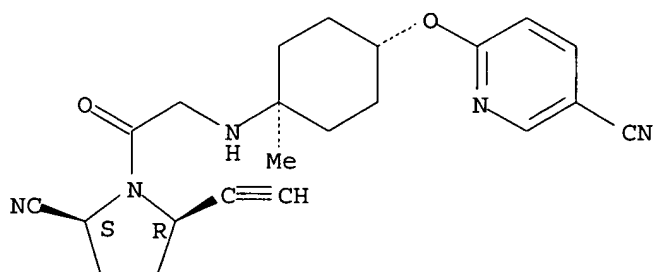
Absolute stereochemistry.



RN 676560-35-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(5-cyano-2-pyridinyl)oxy]-1-methylcyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

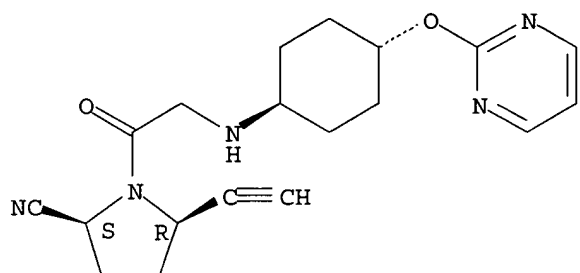
Absolute stereochemistry.



RN 676560-36-4 CAPLUS

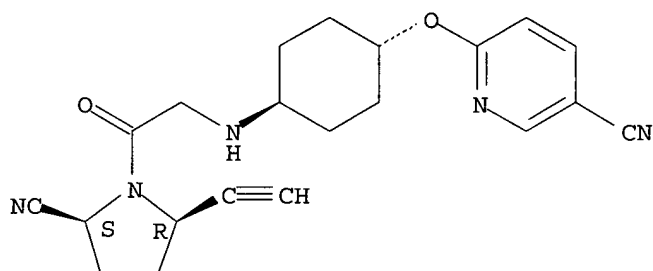
CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-(2-pyrimidinyl)oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



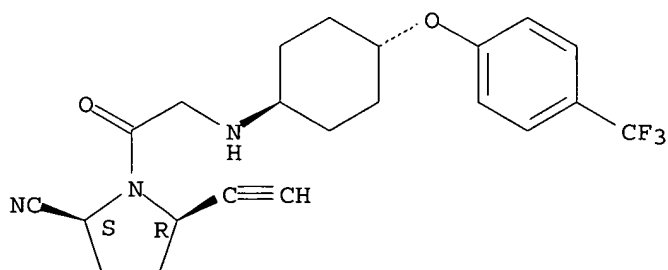
RN 676560-37-5 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(5-cyano-2-pyridinyl)oxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



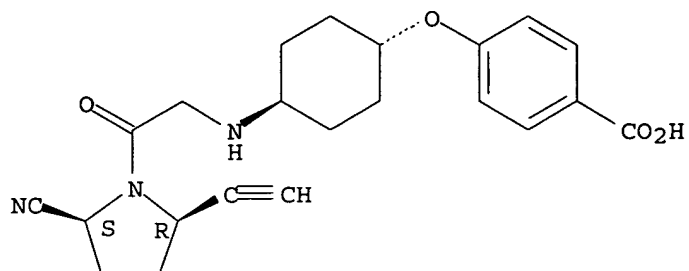
RN 676560-39-7 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[4-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676560-41-1 CAPLUS
 CN Benzoic acid, 4-[[[trans-4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]cyclohexyl]oxy]- (9CI) (CA INDEX NAME)

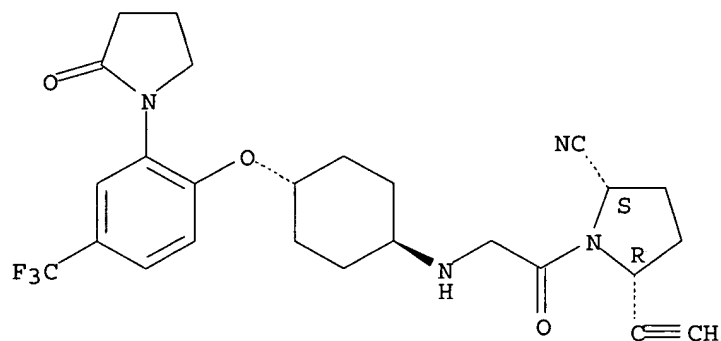
Absolute stereochemistry.



RN 676560-44-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[2-(2-oxo-1-pyrrolidinyl)-4-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)-(9CI) (CA INDEX NAME)

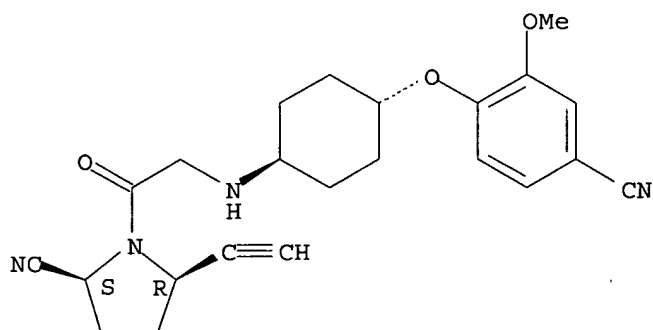
Absolute stereochemistry.



RN 676560-47-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(4-cyano-2-methoxyphenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)-(9CI) (CA INDEX NAME)

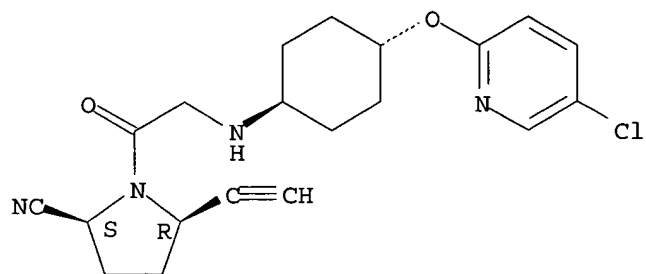
Absolute stereochemistry.



RN 676560-50-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(5-chloro-2-pyridinyl)oxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)-(9CI) (CA INDEX NAME)

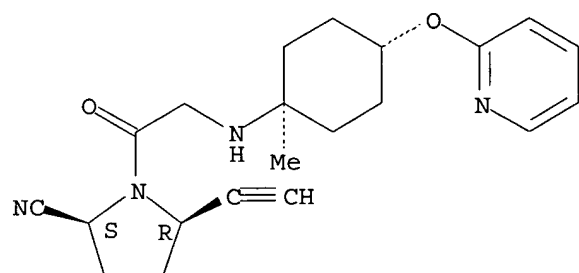
Absolute stereochemistry.



RN 676560-52-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-1-methyl-4-(2-pyridinyloxy)cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

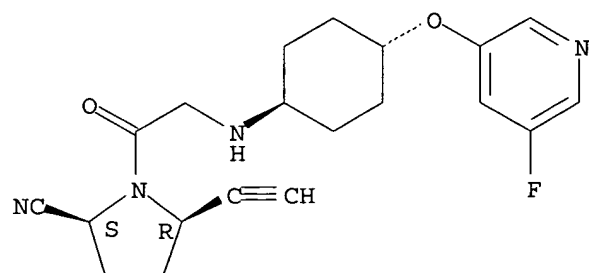
Absolute stereochemistry.



RN 676560-54-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[(5-fluoro-3-pyridinyl)oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

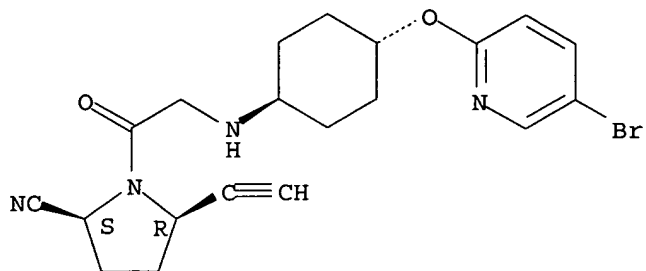
Absolute stereochemistry.



RN 676560-56-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(5-bromo-2-pyridinyl)oxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

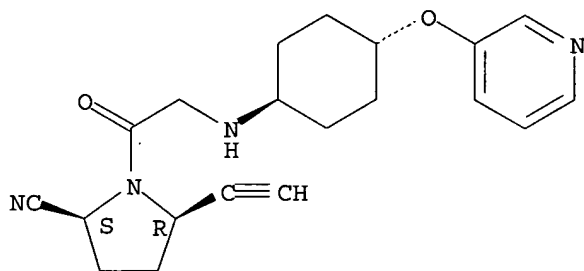
Absolute stereochemistry.



RN 676560-58-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-(3-pyridinyloxy)cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

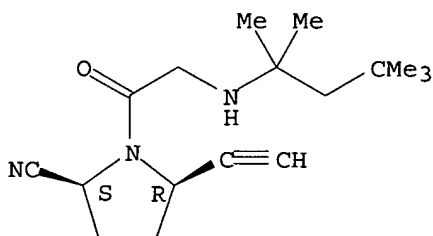
Absolute stereochemistry.



RN 676560-60-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1,1,3,3-tetramethylbutyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

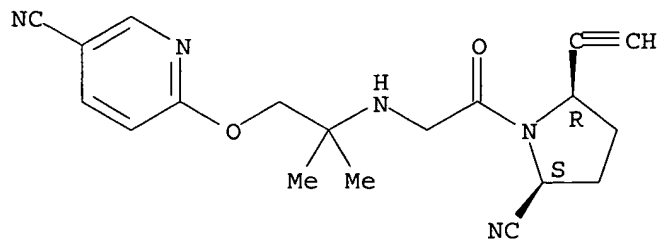
Absolute stereochemistry.



RN 676560-61-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(5-cyano-2-pyridinyl)oxy]-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

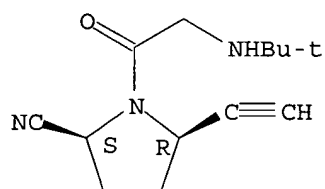
Absolute stereochemistry.



RN 676560-63-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(1,1-dimethylethyl)amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

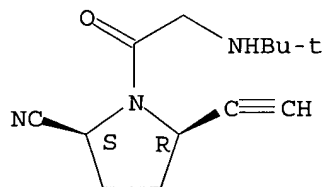
Absolute stereochemistry.



RN 676560-64-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(1,1-dimethylethyl)amino]acetyl]-5-ethynyl-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

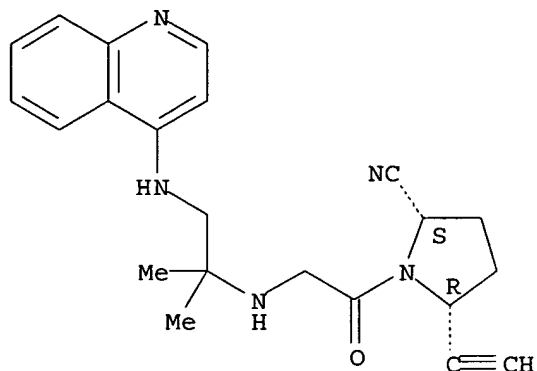


● HCl

RN 676560-65-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1,1-dimethyl-2-(4-quinolinylamino)ethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

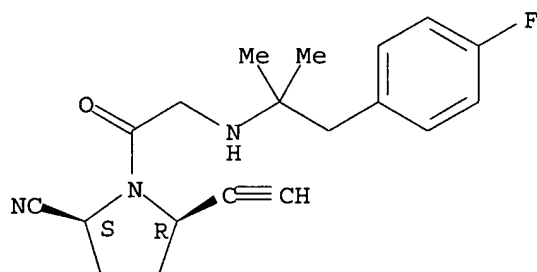
Absolute stereochemistry.



RN 676560-66-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[2-(4-fluorophenyl)-1,1-dimethylethyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

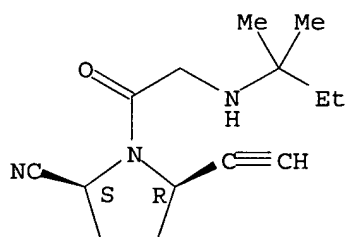
Absolute stereochemistry.



RN 676560-67-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1,1-dimethylpropyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

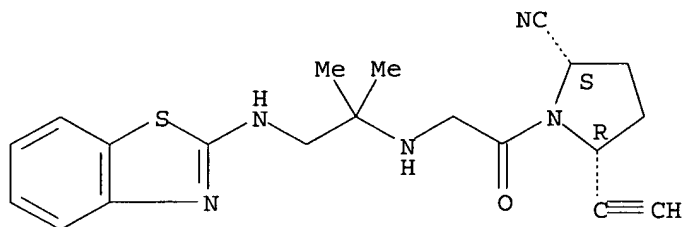
Absolute stereochemistry.



RN 676560-68-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-(2-benzothiazolylamino)-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

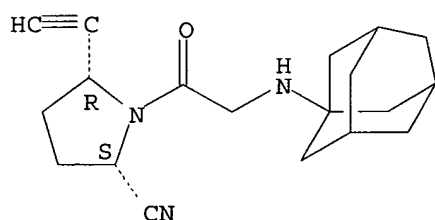
Absolute stereochemistry.



RN 676560-69-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[(tricyclo[3.3.1.1.3,7]dec-1-ylamino)acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

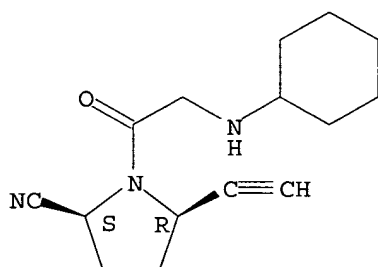
Absolute stereochemistry.



RN 676560-70-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclohexylamino)acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

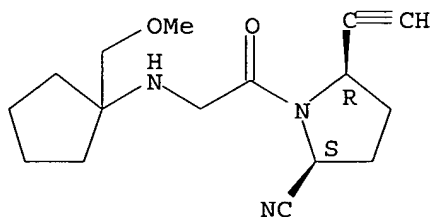
Absolute stereochemistry.



RN 676560-71-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1-(methoxymethyl)cyclopentyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

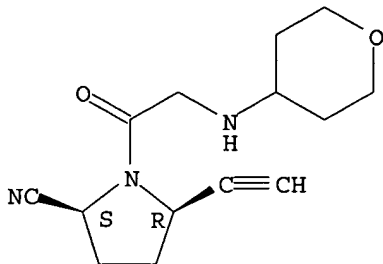
Absolute stereochemistry.



RN 676560-75-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(tetrahydro-2H-pyran-4-yl)amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

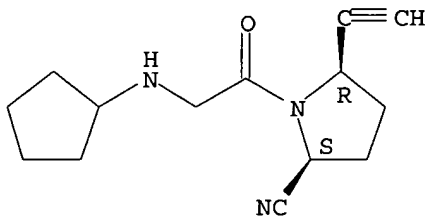
Absolute stereochemistry.



RN 676560-77-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclopentylamino)acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

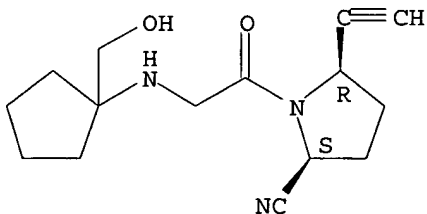
Absolute stereochemistry.



RN 676560-79-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1-(hydroxymethyl)cyclopentyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

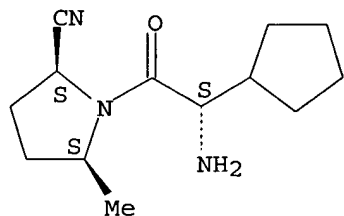
Absolute stereochemistry.



RN 676560-81-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclopentylacetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

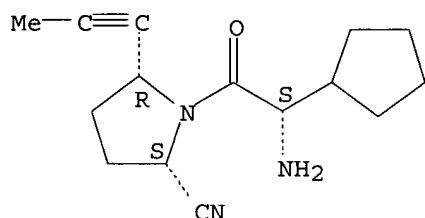
Absolute stereochemistry.



RN 676560-90-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclopentylacetyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

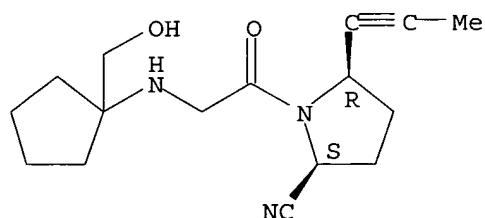
Absolute stereochemistry.



RN 676560-99-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(hydroxymethyl)cyclopentyl]amino]acetyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

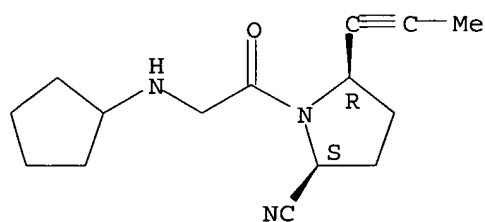
Absolute stereochemistry.



RN 676561-00-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclopentylamino)acetyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

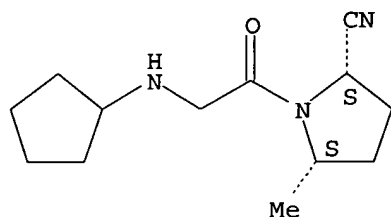
Absolute stereochemistry.



RN 676561-04-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclopentylamino)acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

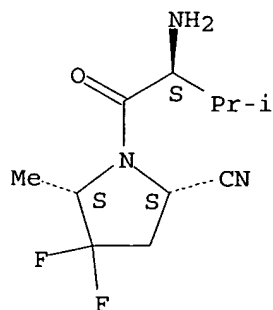
Absolute stereochemistry.



RN 676561-07-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3-methyl-1-oxobutyl]-4,4-difluoro-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

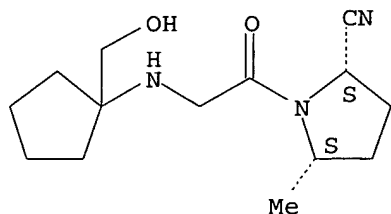
Absolute stereochemistry.



RN 676561-09-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(hydroxymethyl)cyclopentyl]amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

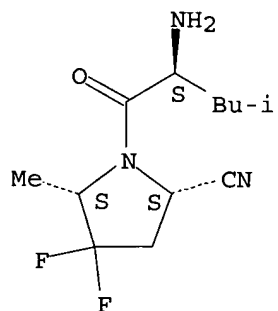
Absolute stereochemistry.



RN 676561-10-7 CAPLUS

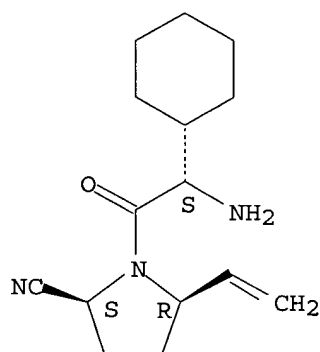
CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-4,4-difluoro-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



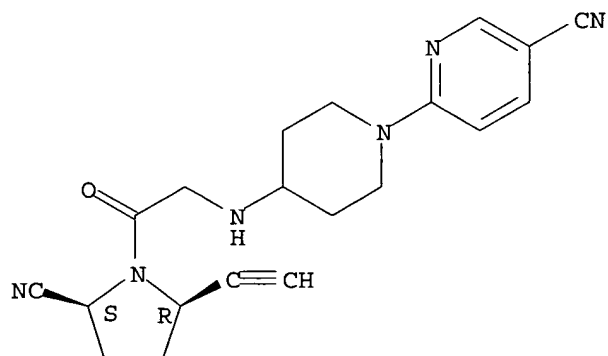
RN 676561-20-9 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclohexylacetyl]-5-ethynyl-,
 (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



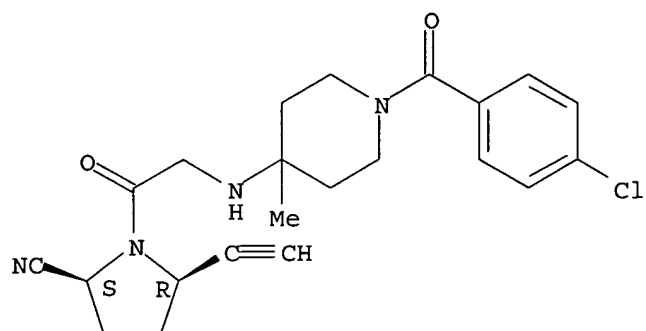
RN 676561-28-7 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-2-pyridinyl)-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676561-29-8 CAPLUS
 CN 4-Piperidinamine, 1-(4-chlorobenzoyl)-N-[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]-4-methyl- (9CI) (CA INDEX NAME)

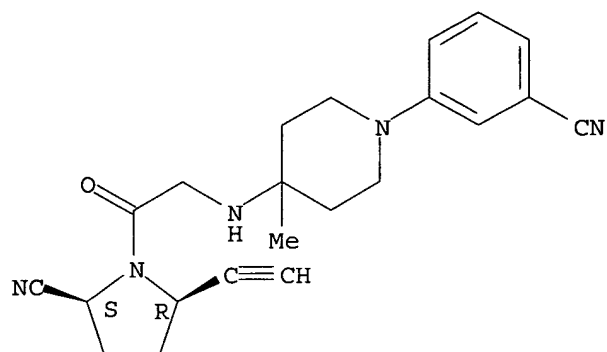
Absolute stereochemistry.



RN 676561-30-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(3-cyanophenyl)-4-methyl-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

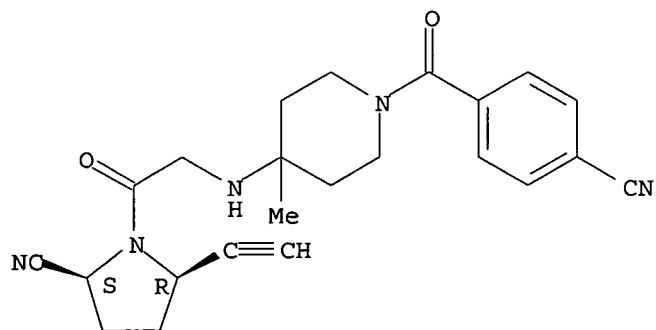
Absolute stereochemistry.



RN 676561-31-2 CAPLUS

CN 4-Piperidinamine, 1-(4-cyanobenzoyl)-N-[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]-4-methyl-, (9CI) (CA INDEX NAME)

Absolute stereochemistry.

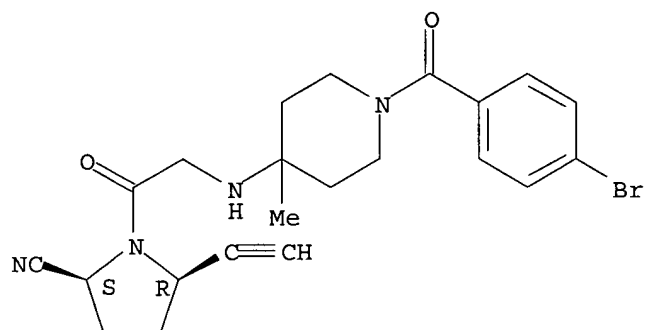


RN 676561-32-3 CAPLUS

CN 4-Piperidinamine, 1-(4-bromobenzoyl)-N-[2-[(2S,5R)-2-cyano-5-ethynyl-1-

pyrrolidinyl]-2-oxoethyl]-4-methyl- (9CI) (CA INDEX NAME)

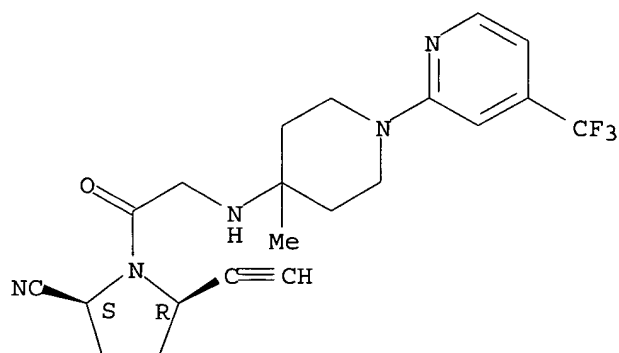
Absolute stereochemistry.



RN 676561-33-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[4-(trifluoromethyl)-2-pyridinyl]-4-piperidinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

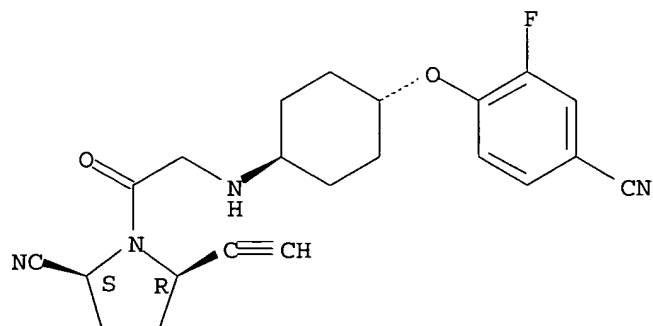
Absolute stereochemistry.



RN 676561-34-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(4-cyano-2-fluorophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

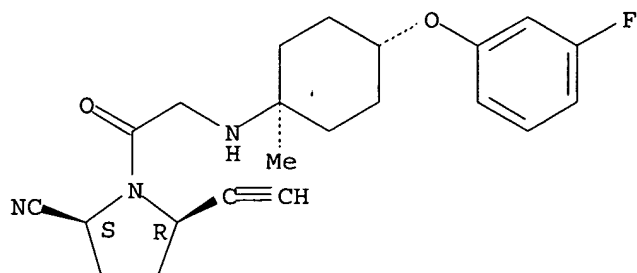
Absolute stereochemistry.



RN 676561-35-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-(3-fluorophenoxy)-1-methylcyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

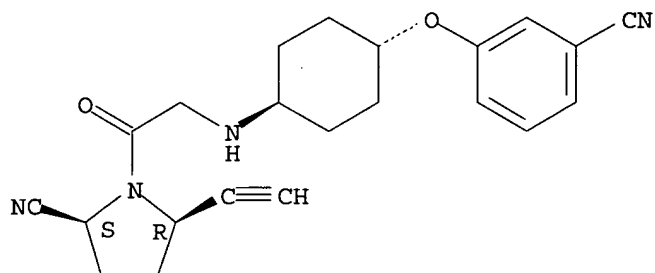
Absolute stereochemistry.



RN 676561-36-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(3-cyanophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

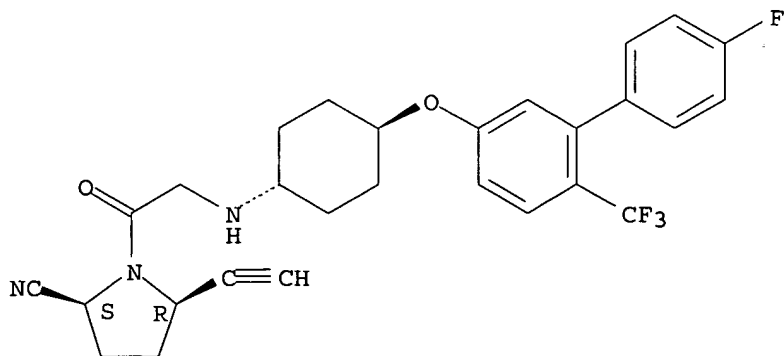
Absolute stereochemistry.



RN 676561-38-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[4'-fluoro-6-(trifluoromethyl)[1,1'-biphenyl]-3-yl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

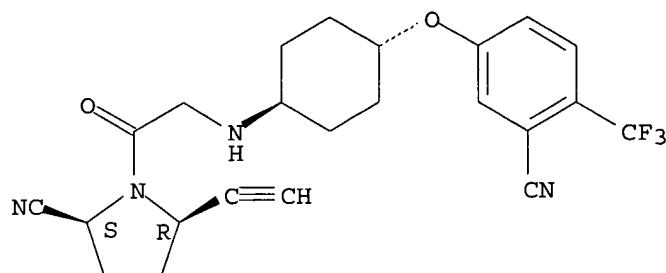
Absolute stereochemistry.



RN 676561-39-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[3-cyano-4-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)-(9CI) (CA INDEX NAME)

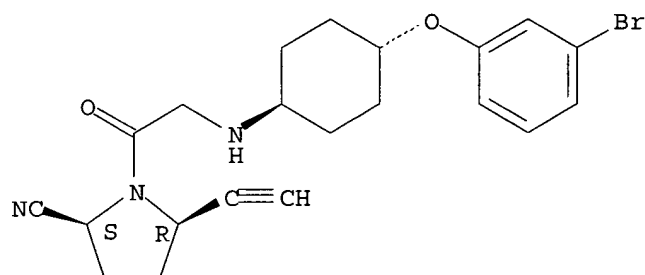
Absolute stereochemistry.



RN 676561-40-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(3-bromophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)-(9CI) (CA INDEX NAME)

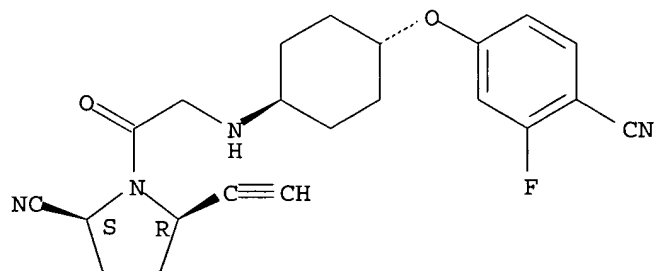
Absolute stereochemistry.



RN 676561-41-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(4-cyano-3-fluorophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)-(9CI) (CA INDEX NAME)

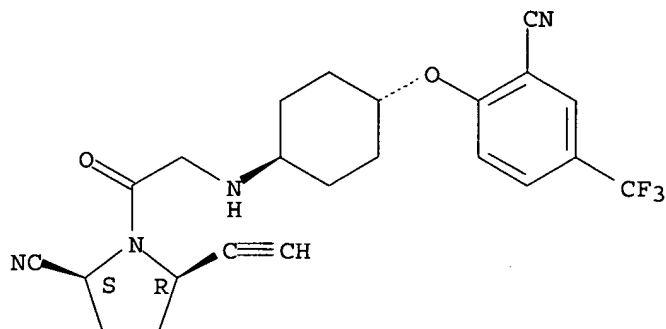
Absolute stereochemistry.



RN 676561-42-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[2-cyano-4-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)-(9CI) (CA INDEX NAME)

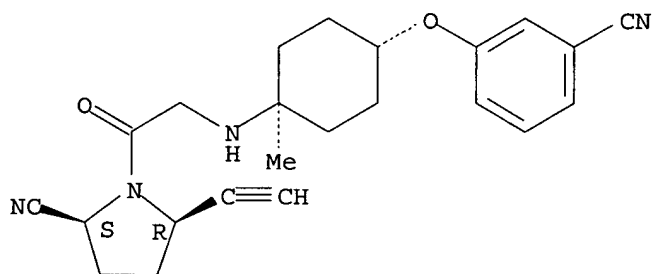
Absolute stereochemistry.



RN 676561-43-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(3-cyanophenoxy)-1-methylcyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

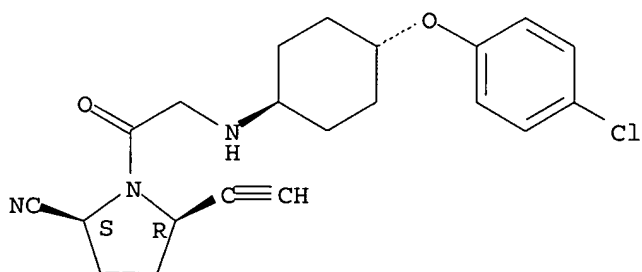
Absolute stereochemistry.



RN 676561-44-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(4-chlorophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

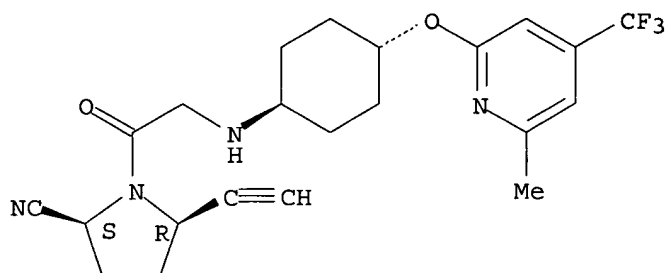
Absolute stereochemistry.



RN 676561-45-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[6-methyl-4-(trifluoromethyl)-2-pyridinyl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

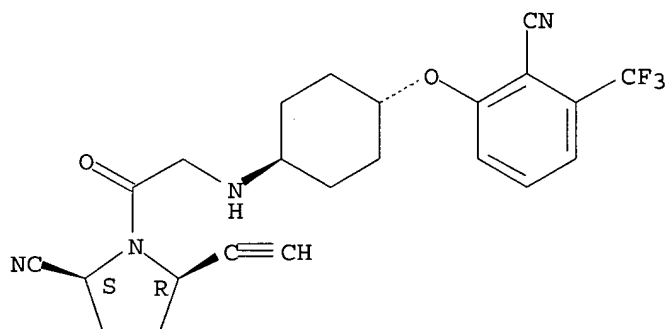
Absolute stereochemistry.



RN 676561-46-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[2-cyano-3-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

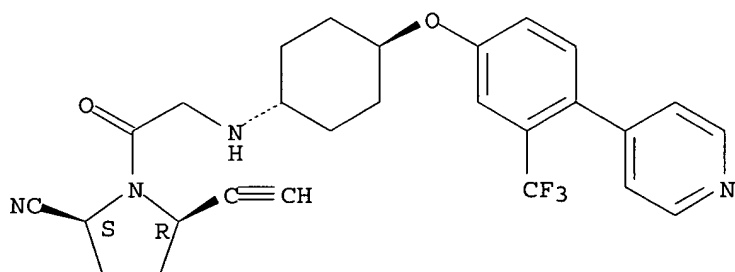
Absolute stereochemistry.



RN 676561-47-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[4-(4-pyridinyl)-3-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

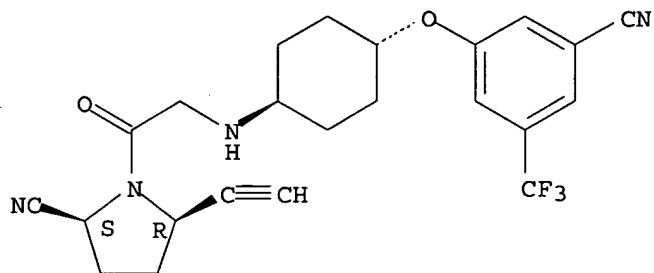
Absolute stereochemistry.



RN 676561-48-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[3-cyano-5-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

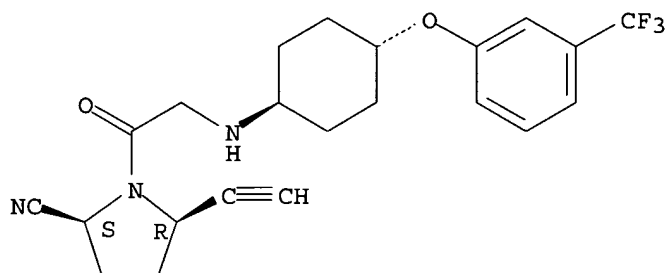
Absolute stereochemistry.



RN 676561-49-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[3-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

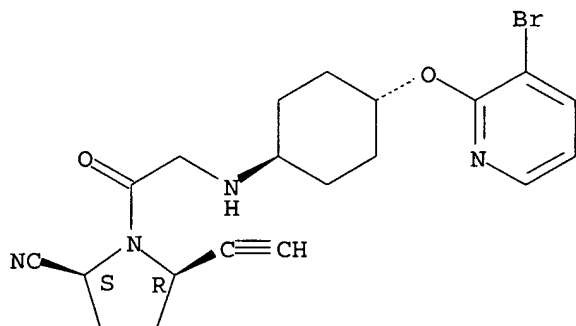
Absolute stereochemistry.



RN 676561-50-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(3-bromo-2-pyridinyl)oxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

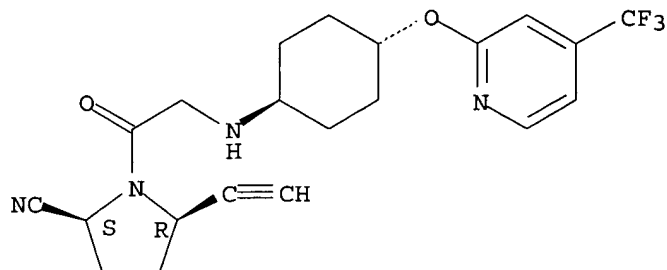
Absolute stereochemistry.



RN 676561-51-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[4-(trifluoromethyl)-2-pyridinyl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

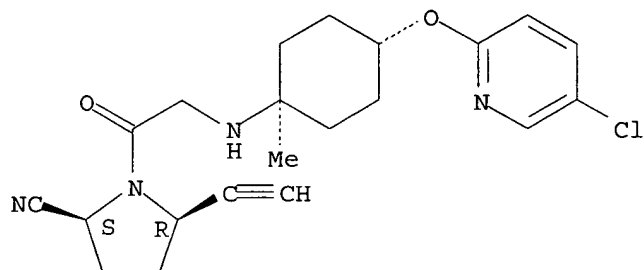
Absolute stereochemistry.



RN 676561-52-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(5-chloro-2-pyridinyl)oxy]-1-methylcyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

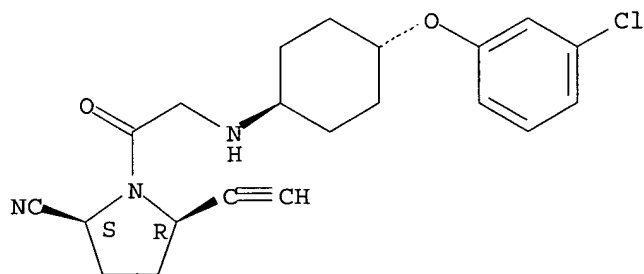
Absolute stereochemistry.



RN 676561-54-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(3-chlorophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

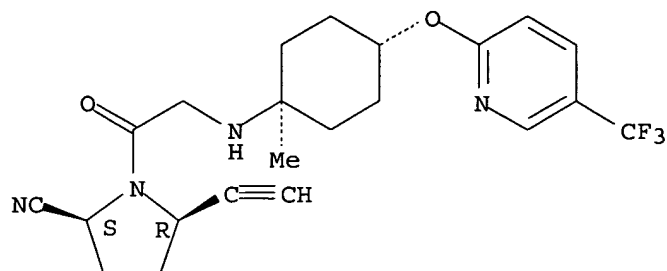
Absolute stereochemistry.



RN 676561-55-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-1-methyl-4-[[5-(trifluoromethyl)-2-pyridinyl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

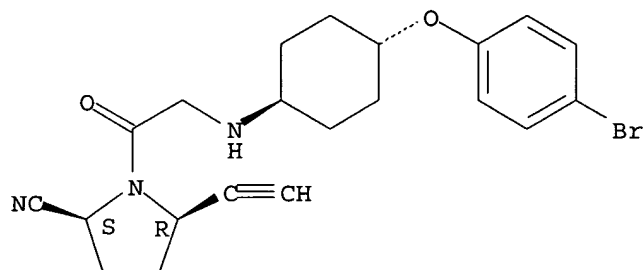
Absolute stereochemistry.



RN 676561-56-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(4-bromophenoxy) cyclohexyl] amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

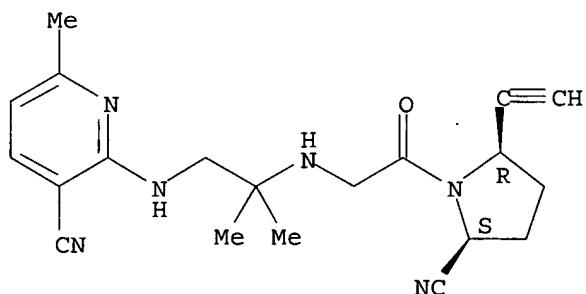
Absolute stereochemistry.



RN 676561-57-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(3-cyano-6-methyl-2-pyridinyl) amino]-1,1-dimethylethyl] amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

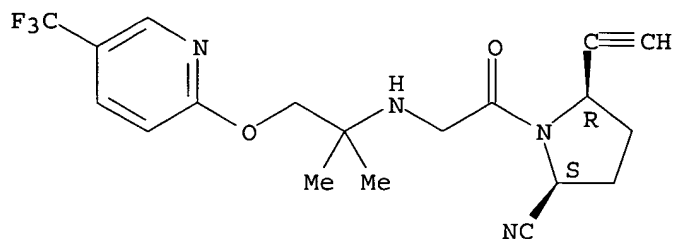
Absolute stereochemistry.



RN 676561-58-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1,1-dimethyl-2-[[5-(trifluoromethyl)-2-pyridinyl]oxy]ethyl] amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

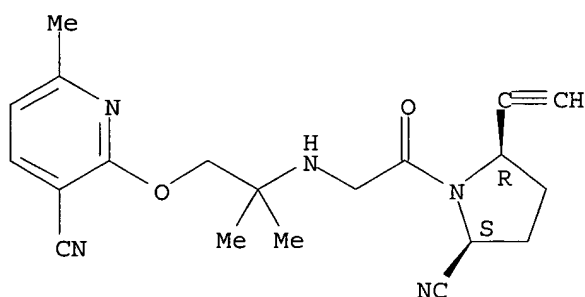
Absolute stereochemistry.



RN 676561-59-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(3-cyano-6-methyl-2-pyridinyl)oxy]-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

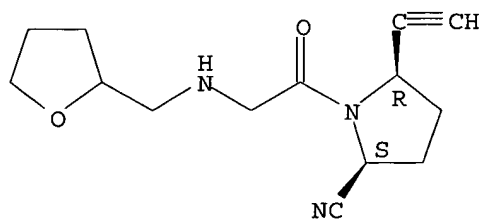
Absolute stereochemistry.



RN 676561-60-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(tetrahydro-2-furanyl)methyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

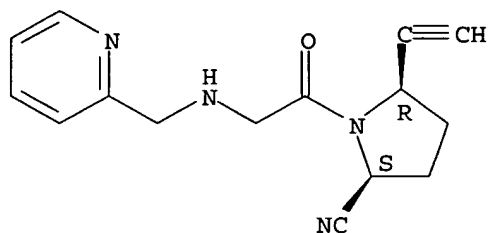
Absolute stereochemistry.



RN 676561-61-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(2-pyridinylmethyl)amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

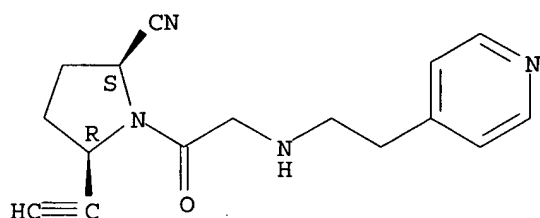
Absolute stereochemistry.



RN 676561-62-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[2-(4-pyridinyl)ethyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

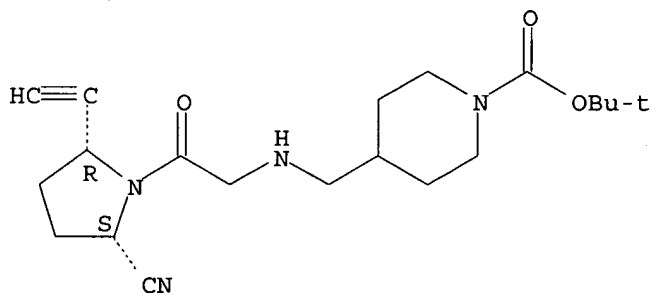
Absolute stereochemistry.



RN 676561-63-0 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

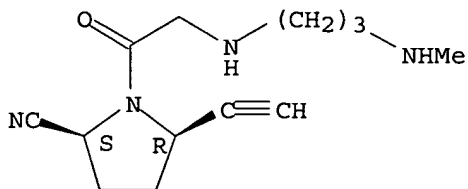
Absolute stereochemistry.



RN 676561-64-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[3-(methylamino)propyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

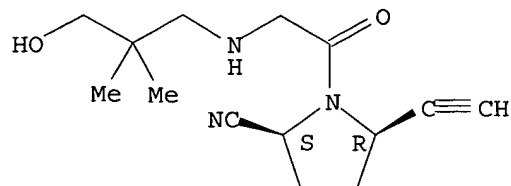
Absolute stereochemistry.



RN 676561-66-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[3-hydroxy-2,2-dimethylpropyl)amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

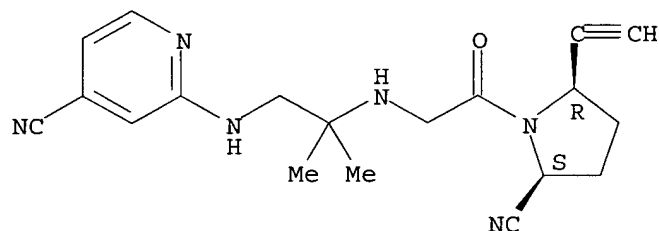
Absolute stereochemistry.



RN 676561-67-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(4-cyano-2-pyridinyl)amino]-1,1-dimethylethyl)amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

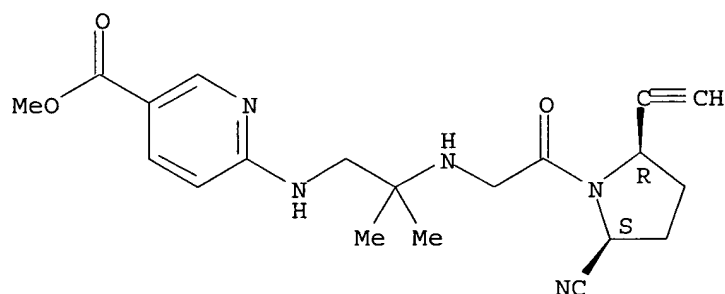
Absolute stereochemistry.



RN 676561-69-6 CAPLUS

CN 3-Pyridinecarboxylic acid, 6-[[2-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-2-methylpropyl]amino]-, methyl ester (9CI) (CA INDEX NAME)

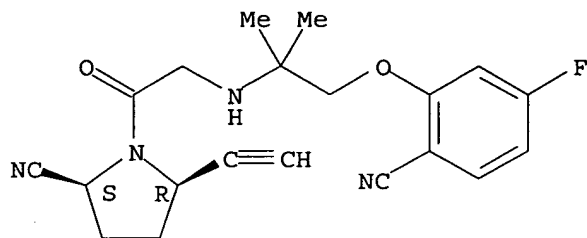
Absolute stereochemistry.



RN 676561-70-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-(2-cyano-5-fluorophenoxy)-1,1-dimethylethyl)amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

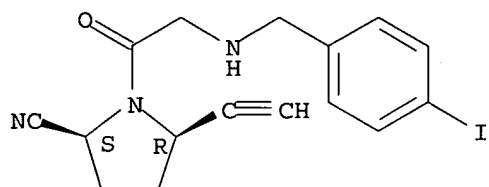
Absolute stereochemistry.



RN 676561-71-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(4-iodophenyl)methyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

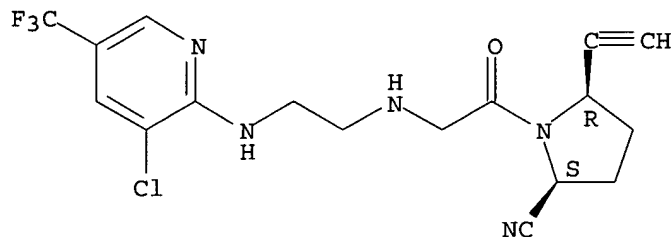
Absolute stereochemistry.



RN 676561-74-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]amino]ethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

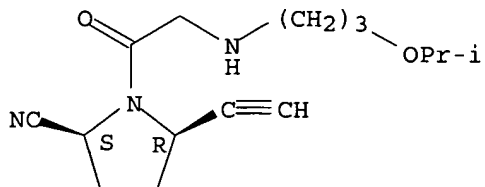
Absolute stereochemistry.



RN 676561-75-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[3-(1-methylethoxy)propyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

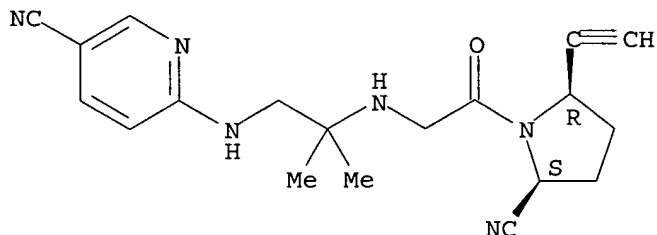
Absolute stereochemistry.



RN 676561-76-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(5-cyano-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

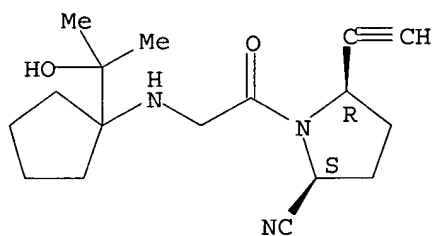
Absolute stereochemistry.



RN 676561-79-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1-(1-hydroxy-1-methylethyl)cyclopentyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

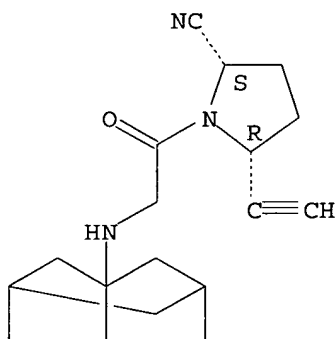
Absolute stereochemistry.



RN 676561-81-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[hexahydro-2,5-methanopentalen-3a(1H)-yl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

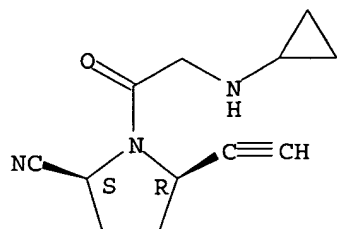
Absolute stereochemistry.



RN 676561-83-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclopropylamino)acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

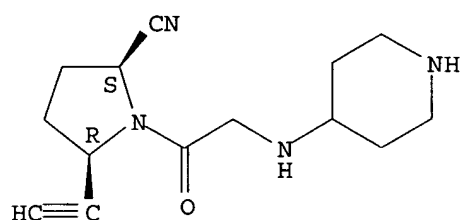
Absolute stereochemistry.



RN 676561-84-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[(4-piperidinylamino)acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

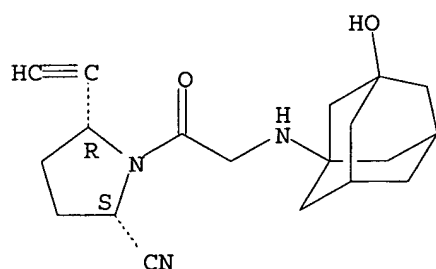
Absolute stereochemistry.



RN 676561-85-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(3-hydroxytricyclo[3.3.1.1^{3,7}]dec-1-yl)amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

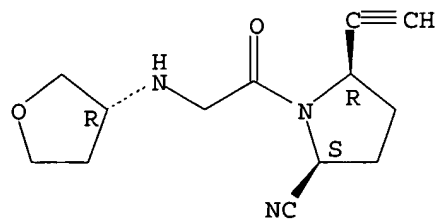
Absolute stereochemistry.



RN 676561-86-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(3R)-tetrahydro-3-furanyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

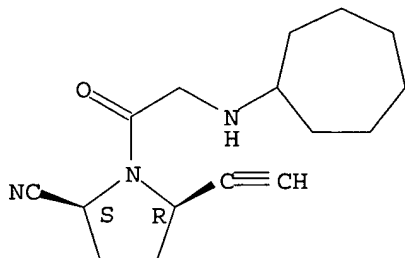
Absolute stereochemistry.



RN 676561-87-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cycloheptylamino)acetyl]-5-ethynyl-,
(2S,5R)- (9CI) (CA INDEX NAME)

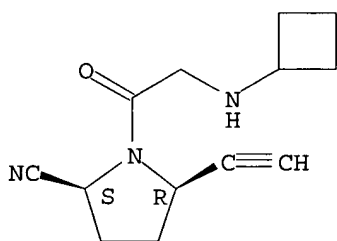
Absolute stereochemistry.



RN 676561-88-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclobutylamino)acetyl]-5-ethynyl-,
(2S,5R)- (9CI) (CA INDEX NAME)

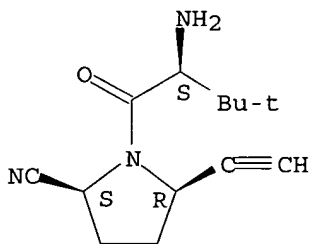
Absolute stereochemistry.



RN 676561-89-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

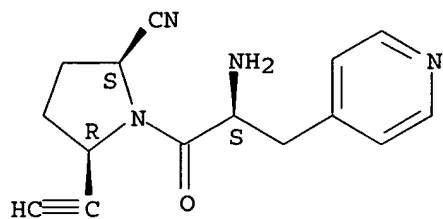
Absolute stereochemistry.



RN 676561-90-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-1-oxo-3-(4-pyridinyl)propyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

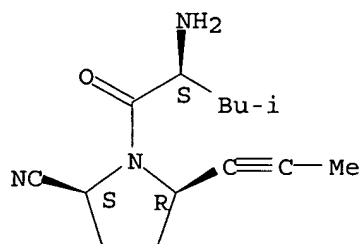
Absolute stereochemistry.



RN 676561-92-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

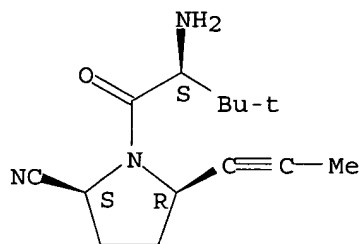
Absolute stereochemistry.



RN 676561-93-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

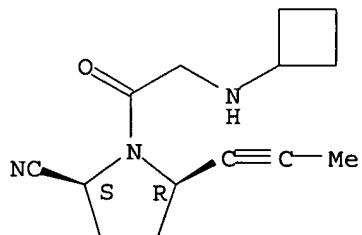
Absolute stereochemistry.



RN 676561-94-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclobutylamino)acetyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

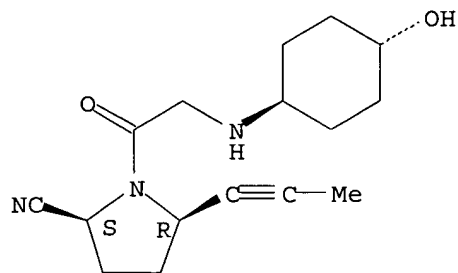
Absolute stereochemistry.



RN 676561-95-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(trans-4-hydroxycyclohexyl)amino]acetyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

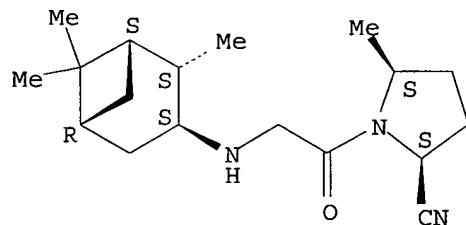
Absolute stereochemistry.



RN 676561-97-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-methyl-1-[[[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino]acetyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

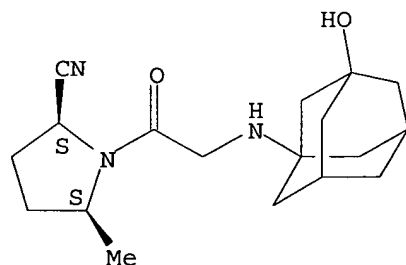
Absolute stereochemistry.



RN 676561-98-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-hydroxytricyclo[3.3.1.1^{3,7}]dec-1-yl)amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

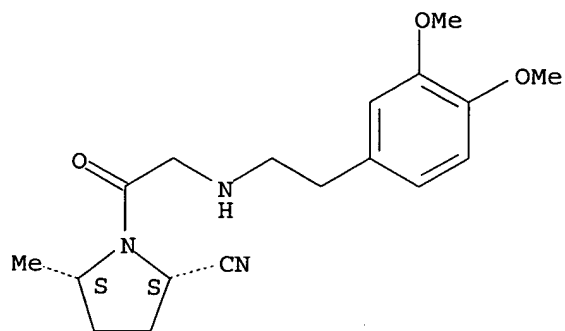
Absolute stereochemistry.



RN 676561-99-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-(3,4-dimethoxyphenyl)ethyl]amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

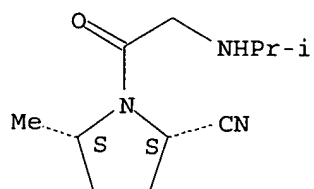
Absolute stereochemistry.



RN 676562-02-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-methyl-1-[[[(1-methylethyl)amino]acetyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

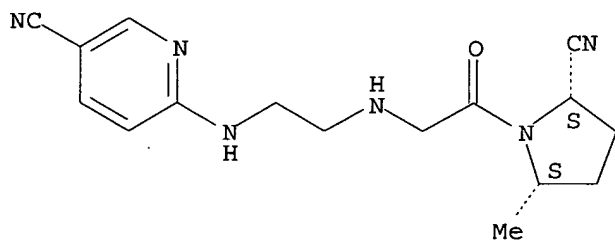
Absolute stereochemistry.



RN 676562-04-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(5-cyano-2-pyridinyl)amino]ethyl]amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

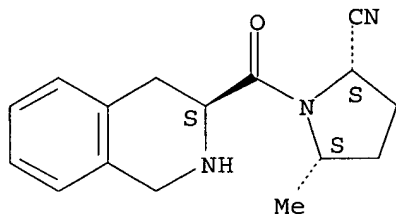
Absolute stereochemistry.



RN 676562-05-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-methyl-1-[[[(3S)-1,2,3,4-tetrahydro-3-isoquinolinyl]carbonyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

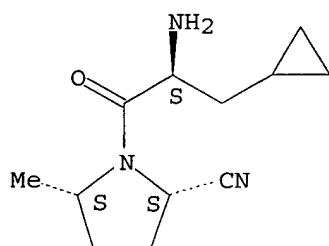
Absolute stereochemistry.



RN 676562-06-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3-cyclopropyl-1-oxopropyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

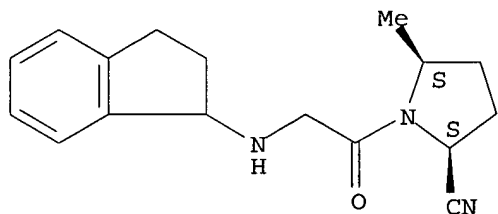
Absolute stereochemistry.



RN 676562-08-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(2,3-dihydro-1H-inden-1-yl)amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

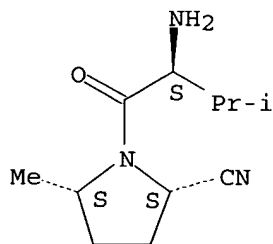
Absolute stereochemistry.



RN 676562-09-7 CAPLUS

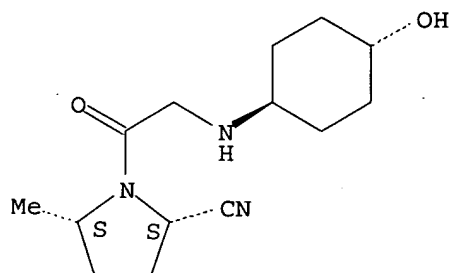
CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3-methyl-1-oxobutyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



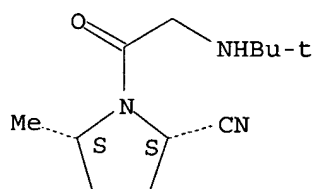
RN 676562-10-0 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[[[(trans-4-hydroxycyclohexyl)amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



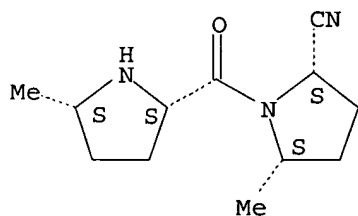
RN 676562-11-1 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[[[(1,1-dimethylethyl)amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



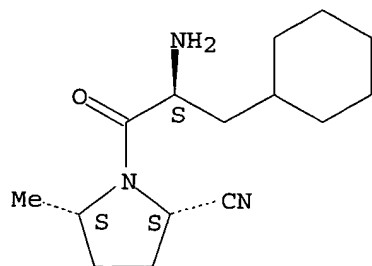
RN 676562-12-2 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 5-methyl-1-[[[(2S,5S)-5-methyl-2-pyrrolidinyl]carbonyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676562-13-3 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3-cyclohexyl-1-oxopropyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

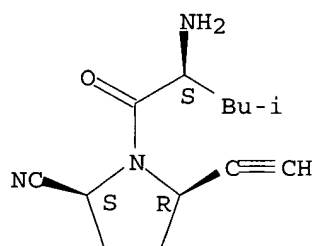
Absolute stereochemistry.



RN 676562-14-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-5-ethynyl-, (2S,5R)-(9CI) (CA INDEX NAME)

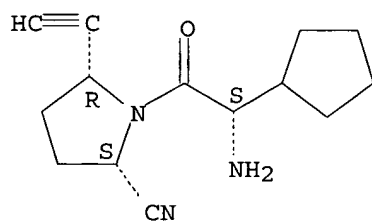
Absolute stereochemistry.



RN 676562-15-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclopentylacetyl]-5-ethynyl-, (2S,5R)-(9CI) (CA INDEX NAME)

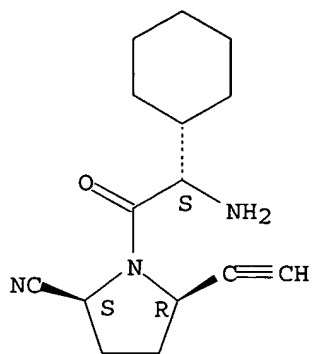
Absolute stereochemistry.



RN 676562-18-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclohexylacetyl]-5-ethynyl-, (2S,5R)-(9CI) (CA INDEX NAME)

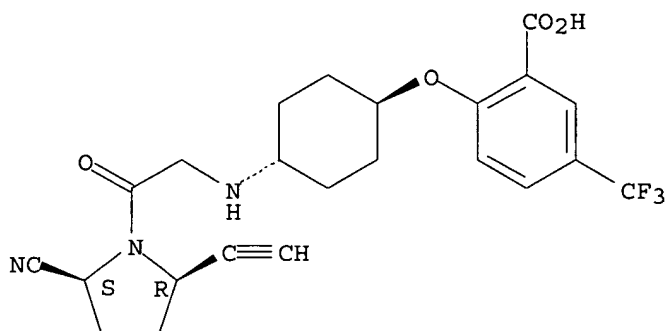
Absolute stereochemistry.



RN 676562-22-4 CAPLUS

CN Benzoic acid, 2-[[[trans-4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]cyclohexyl]oxy]-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)

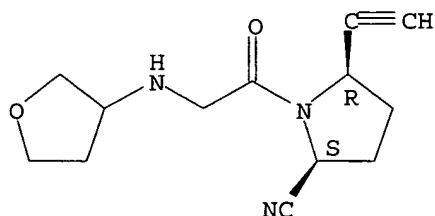
Absolute stereochemistry.



RN 676562-24-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[tetrahydro-3-furanyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

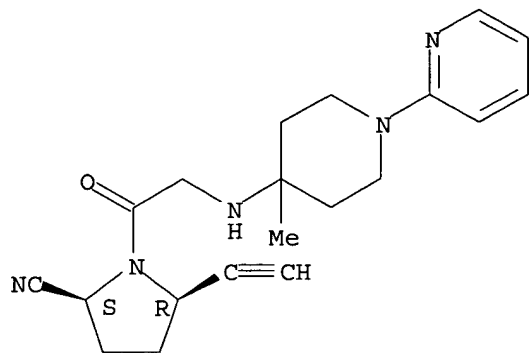
Absolute stereochemistry.



RN 676562-25-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-(2-pyridinyl)-4-piperidinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

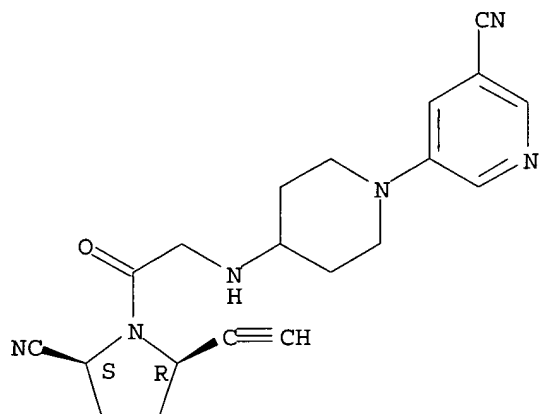
Absolute stereochemistry.



RN 676562-26-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-3-pyridinyl)-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

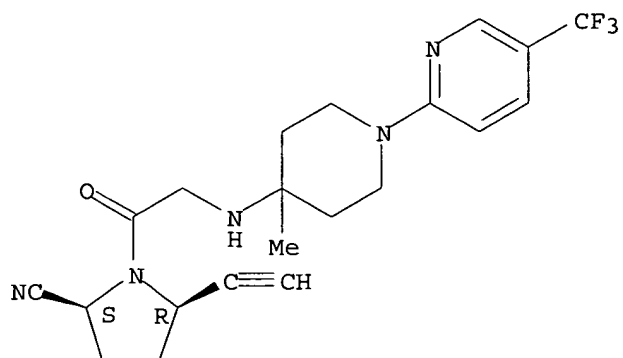
Absolute stereochemistry.



RN 676562-27-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[5-(trifluoromethyl)-2-pyridinyl]-4-piperidinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

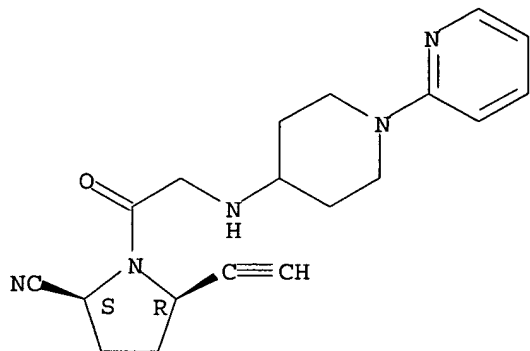
Absolute stereochemistry.



RN 676562-28-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1-(2-pyridinyl)-4-piperidinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

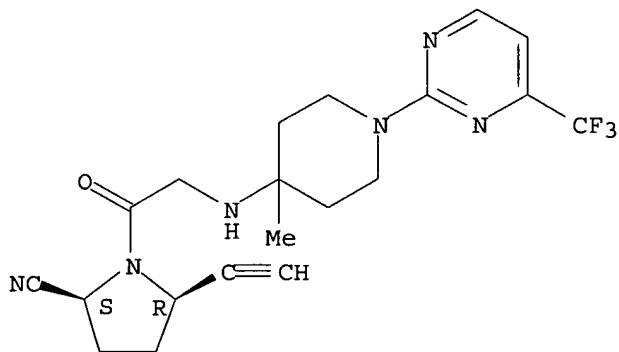
Absolute stereochemistry.



RN 676562-29-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[4-(trifluoromethyl)-2-pyrimidinyl]-4-piperidinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

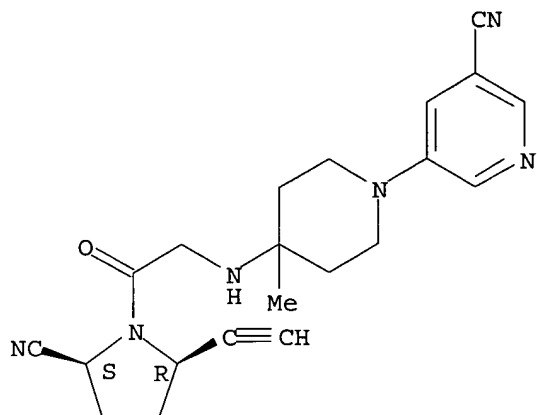
Absolute stereochemistry.



RN 676562-30-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-3-pyridinyl)-4-methyl-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

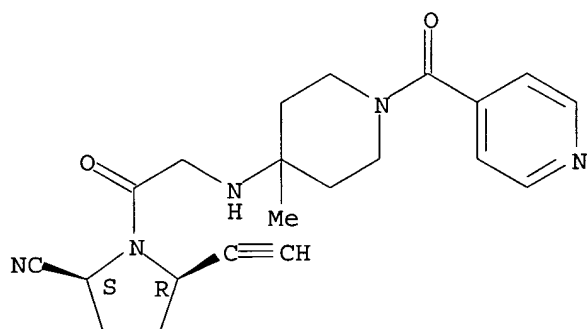
Absolute stereochemistry.



RN 676562-31-5 CAPLUS

CN 4-Piperidinamine, N-[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]-4-methyl-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

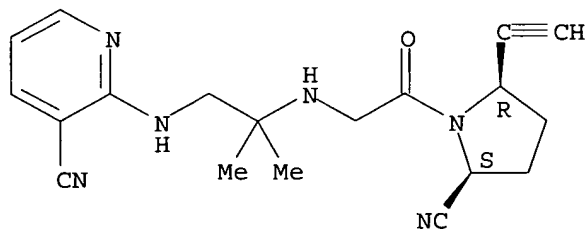
Absolute stereochemistry.



RN 676562-32-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(3-cyano-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

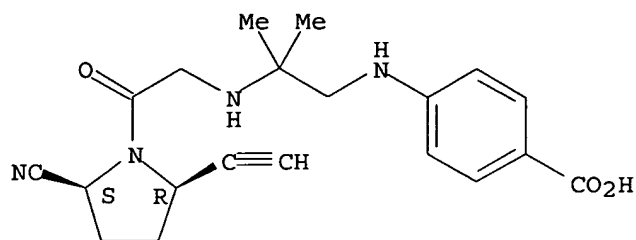
Absolute stereochemistry.



RN 676562-33-7 CAPLUS

CN Benzoic acid, 4-[[2-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-2-methylpropyl]amino]- (9CI) (CA INDEX NAME)

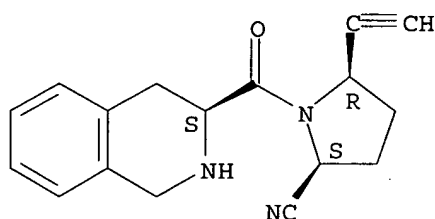
Absolute stereochemistry.



RN 676562-34-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(3S)-1,2,3,4-tetrahydro-3-isoquinoliny]carbonyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

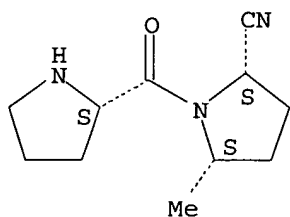
Absolute stereochemistry.



RN 676562-35-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-methyl-1-[(2S)-2-pyrrolidinylcarbonyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

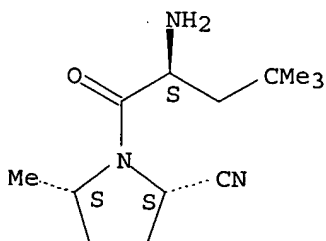
Absolute stereochemistry.



RN 676565-48-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4,4-dimethyl-1-oxopentyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

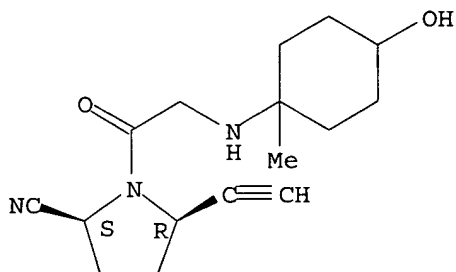
Absolute stereochemistry.



RN 676597-84-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-hydroxy-1-methylcyclohexyl)amino]acetyl]-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

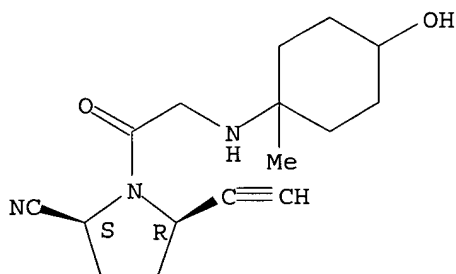


● HCl

RN 676597-85-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-hydroxy-1-methylcyclohexyl)amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

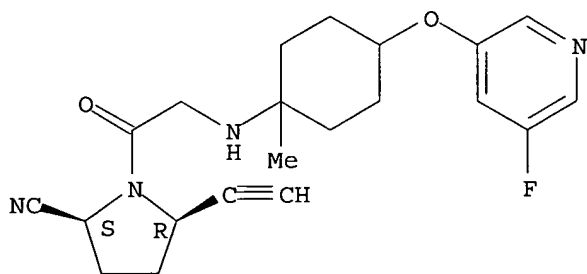
Absolute stereochemistry.



RN 676597-86-7 CAPLUS

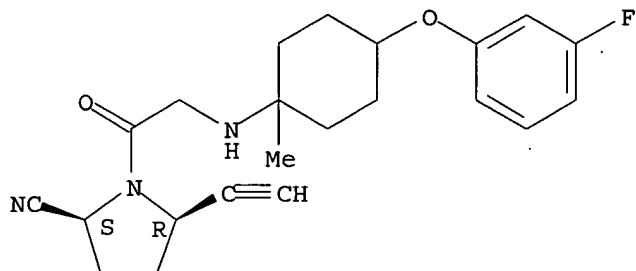
CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-[(5-fluoro-3-pyridinyl)oxy]-1-methylcyclohexyl)amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



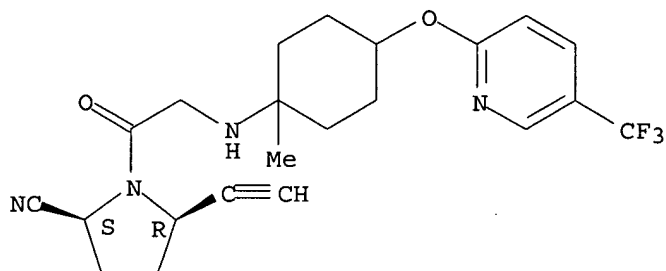
RN 676597-88-9 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-(3-fluorophenoxy)-1-methylcyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



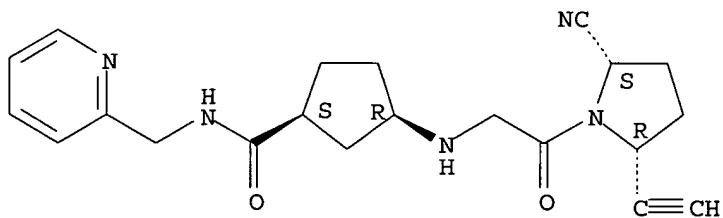
RN 676597-89-0 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1-methyl-4-[[5-(trifluoromethyl)-2-pyridinyl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



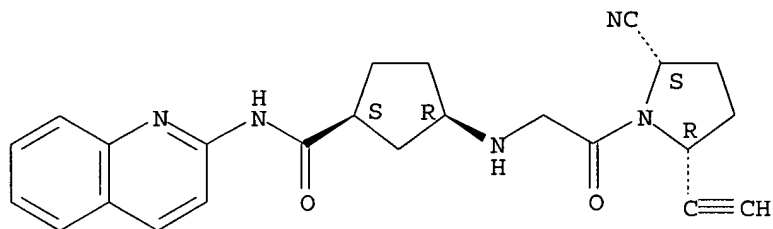
RN 813433-87-3 CAPLUS
 CN Cyclopentanecarboxamide, 3-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-N-(2-pyridinylmethyl)-, (1S,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 813433-88-4 CAPLUS
 CN Cyclopentanecarboxamide, 3-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-N-2-quinolinyl-, (1S,3R)- (9CI) (CA INDEX NAME)

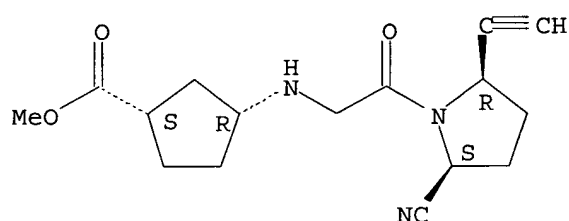
Absolute stereochemistry.



RN 813433-91-9 CAPLUS

CN Cyclopentanecarboxylic acid, 3-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-, methyl ester, (1S,3R)- (9CI) (CA INDEX NAME)

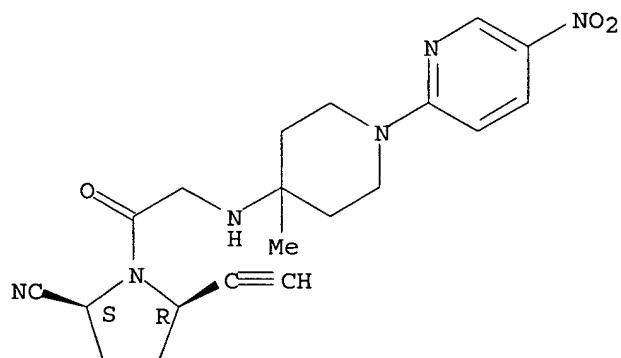
Absolute stereochemistry.



RN 813434-08-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-(5-nitro-2-pyridinyl)-4-piperidinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

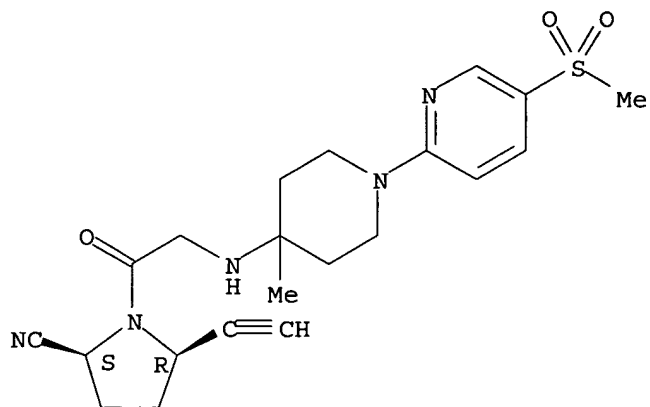
Absolute stereochemistry.



RN 813434-10-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[5-(methylsulfonyl)-2-pyridinyl]-4-piperidinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

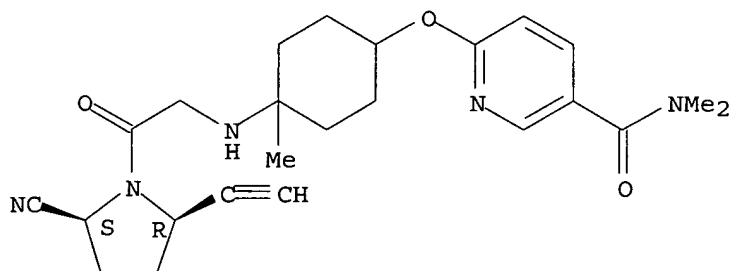
Absolute stereochemistry.



RN 815578-56-4 CAPLUS

CN 3-Pyridinecarboxamide, 6-[[4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-4-methylcyclohexyl]oxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)

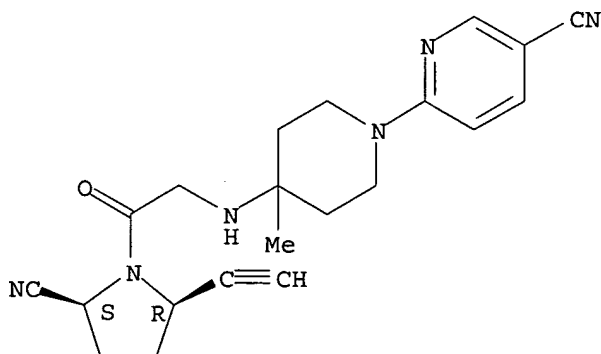
Absolute stereochemistry.



RN 865980-24-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-2-pyridinyl)-4-methyl-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

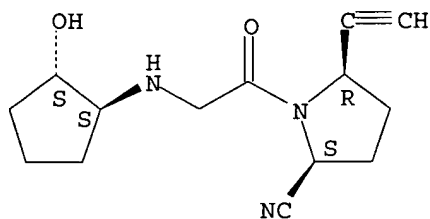


RN 865980-25-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(1S,2S)-2-[[4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-4-methylcyclohexyl]oxy]-4-(cyano)pyridin-3-yl]amino]acetyl]-, (1S,2S)- (9CI) (CA INDEX NAME)

hydroxycyclopentyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

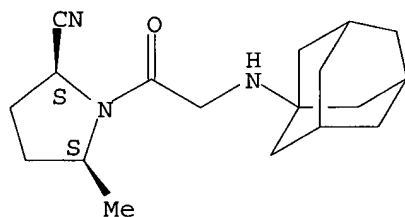
Absolute stereochemistry.



RN 865980-26-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-methyl-1-[(tricyclo[3.3.1.1.3,7]dec-1-ylamino)acetyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

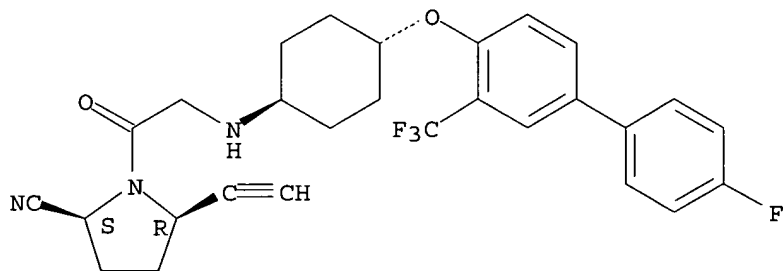
Absolute stereochemistry.



RN 865980-27-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[4'-fluoro-3-(trifluoromethyl)[1,1'-biphenyl]-4-yl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

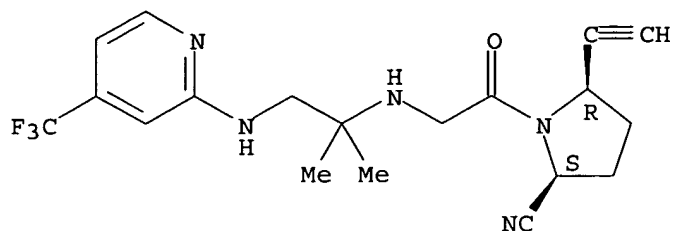
Absolute stereochemistry.



RN 865980-29-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1,1-dimethyl-2-[[4-(trifluoromethyl)-2-pyridinyl]amino]ethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

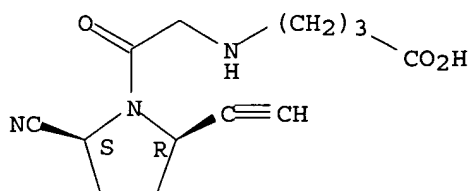
Absolute stereochemistry.



RN 865980-30-9 CAPLUS

CN Butanoic acid, 4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

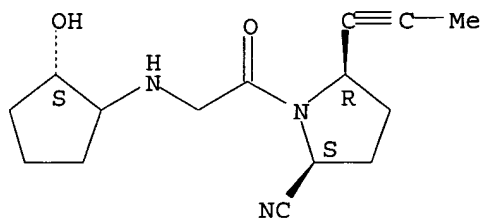
Absolute stereochemistry.



RN 865980-32-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(2S)-2-hydroxycyclopentyl]amino]acetyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

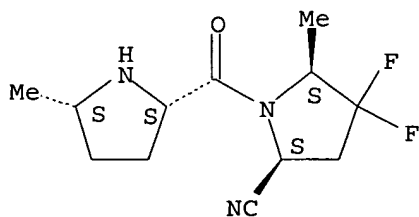
Absolute stereochemistry.



RN 865980-33-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-5-methyl-1-[[[(2S,5S)-5-methyl-2-pyrrolidinyl]carbonyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

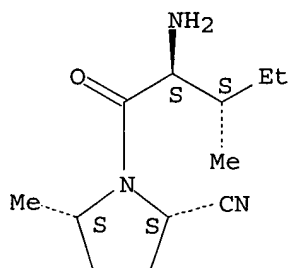


RN 865980-34-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-5- (9CI) (CA INDEX NAME)

methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

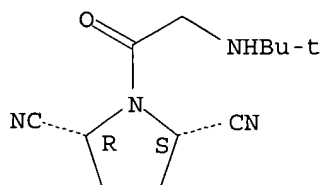
Absolute stereochemistry.



RN 865980-35-4 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[(1,1-dimethylethyl)amino]acetyl]-, (2R,5S)- (9CI) (CA INDEX NAME)

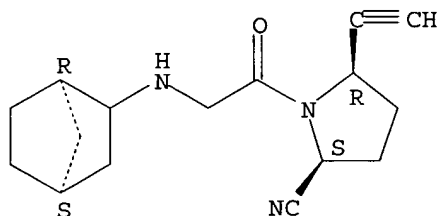
Absolute stereochemistry.



RN 865980-36-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(1R,4S)-bicyclo[2.2.1]hept-2-ylamino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 865980-40-1 CAPLUS

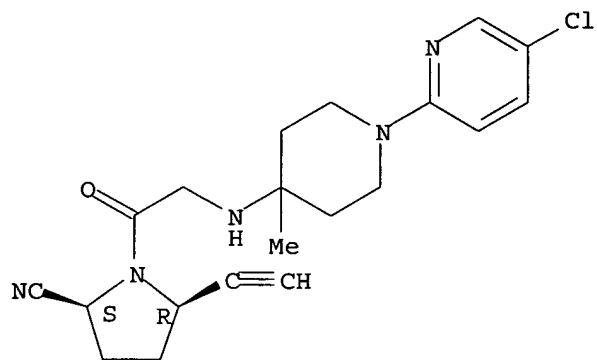
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-chloro-2-pyridinyl)-4-methyl-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 676559-88-9

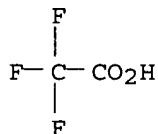
CMF C20 H24 Cl N5 O

Absolute stereochemistry.



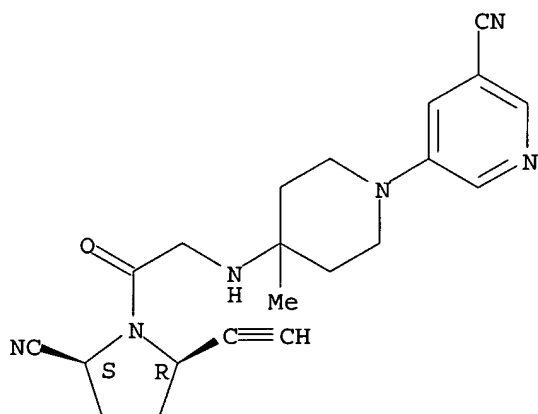
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 865980-41-2 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-3-pyridinyl)-4-methyl-4-piperidinyl]amino]acetyl]-5-ethynyl-, monohydrochloride, (2S,5R)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

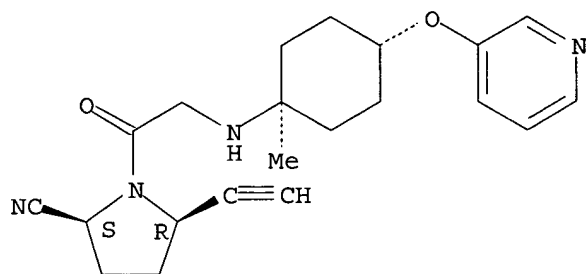


● HCl

RN 865980-42-3 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-1-methyl-4-(3-

pyridinyloxy)cyclohexyl]amino]acetyl]-, monohydrochloride, (2S,5R)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

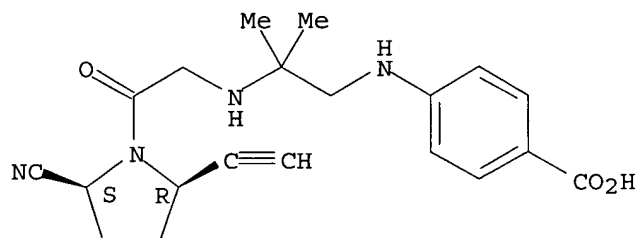


● HCl

RN 865980-51-4 CAPLUS

CN Benzoic acid, 4-[[2-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-2-methylpropyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

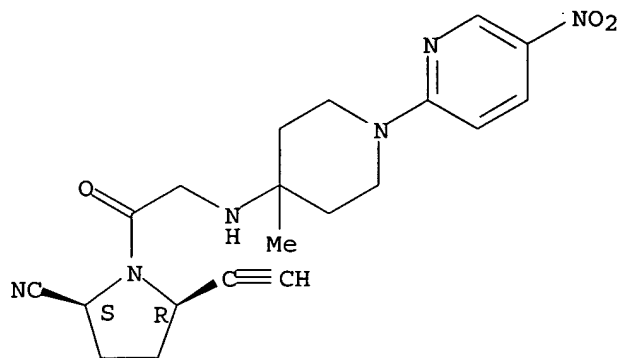


● HCl

RN 865980-52-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-(5-nitro-2-pyridinyl)-4-piperidinyl]amino]acetyl]-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

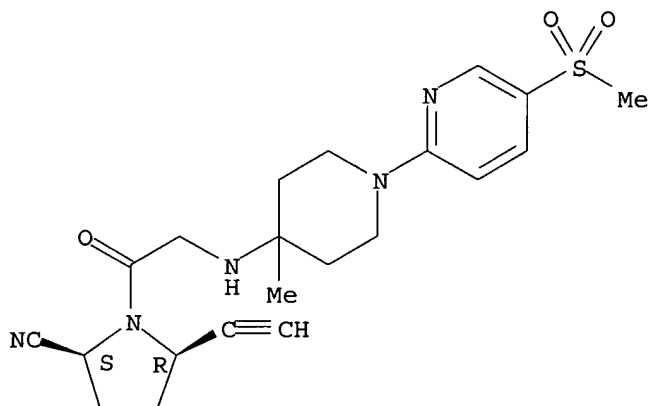


● HCl

RN 865980-53-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[5-(methanesulfonyl)-2-pyridinyl]-4-piperidinyl]amino]acetyl]-, monohydrochloride, (2S,5R)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

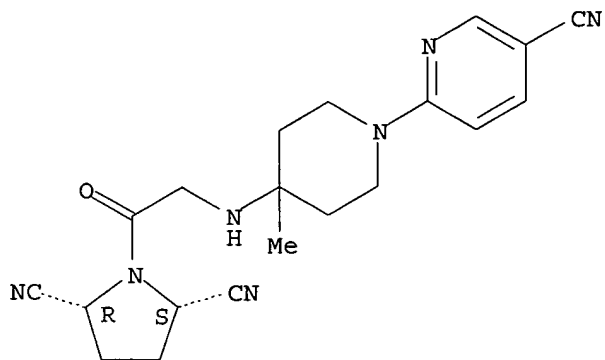


● HCl

RN 865980-56-9 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[1-(5-cyano-2-pyridinyl)-4-methyl-4-piperidinyl]amino]acetyl]-, monohydrochloride, (2R,5S)- (9CI) (CA INDEX NAME)

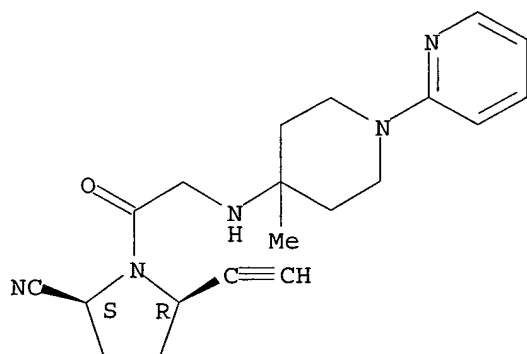
Absolute stereochemistry.



● HCl

RN 865980-57-0 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-(2-pyridinyl)-4-piperidinyl]amino]acetyl]-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

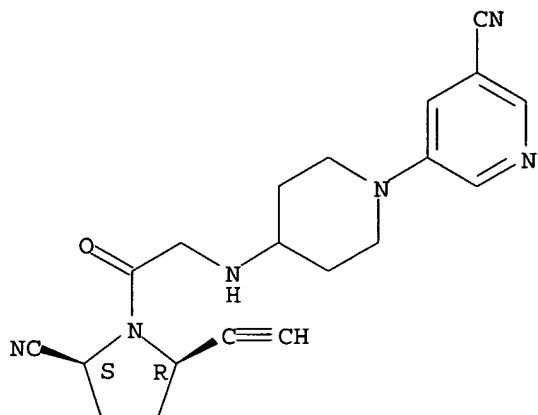
Absolute stereochemistry.



● HCl

RN 865980-58-1 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-3-pyridinyl)-4-piperidinyl]amino]acetyl]-5-ethynyl-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

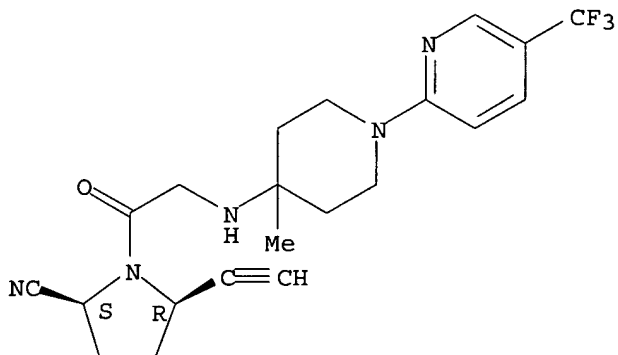


● HCl

RN 865980-59-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[5-(trifluoromethyl)-2-pyridinyl]-4-piperidinyl]amino]acetyl]-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

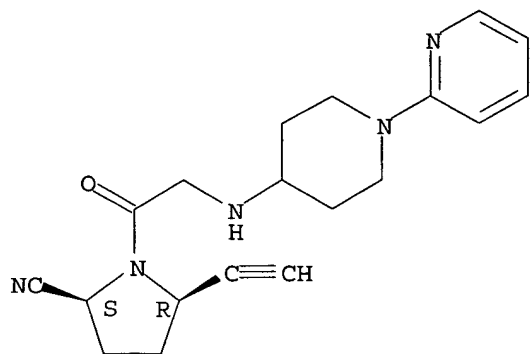


● HCl

RN 865980-60-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1-(2-pyridinyl)-4-piperidinyl]amino]acetyl]-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

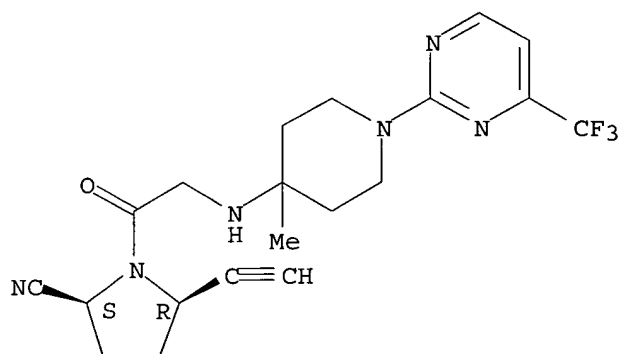
Absolute stereochemistry.



● HCl

RN 865980-61-6 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[4-(trifluoromethyl)-2-pyrimidinyl]-4-piperidinyl]amino]acetyl]-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

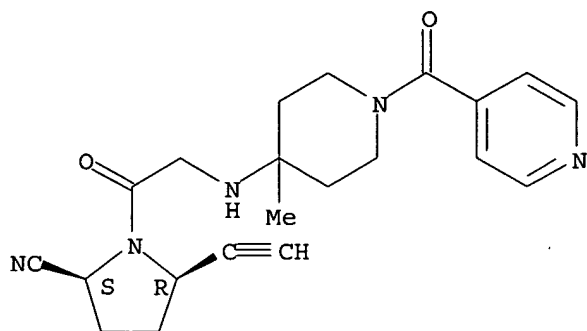
Absolute stereochemistry.



● HCl

RN 865980-62-7 CAPLUS
 CN 4-Piperidinamine, N-[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]-4-methyl-1-(4-pyridinylcarbonyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

RN 865980-63-8 CAPLUS

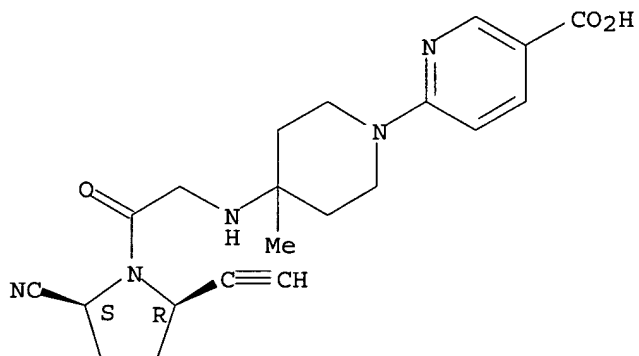
CN 3-Pyridinecarboxylic acid, 6-[4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-4-methyl-1-piperidinyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 676559-99-2

CMF C21 H25 N5 O3

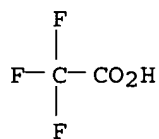
Absolute stereochemistry.



CM 2

CRN 76-05-1

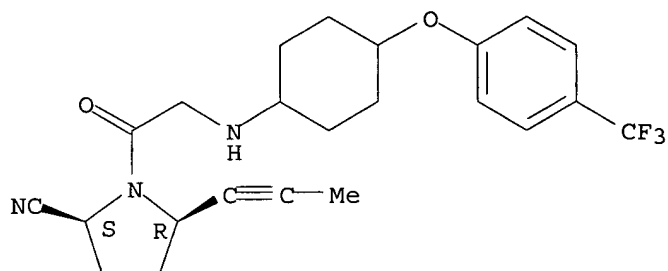
CMF C2 H F3 O2



RN 866012-65-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-(1-propynyl)-1-[[[4-[4-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

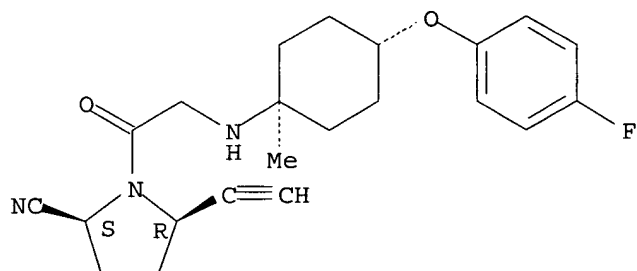
Absolute stereochemistry.



RN 866012-66-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-(4-fluorophenoxy)-1-methylcyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

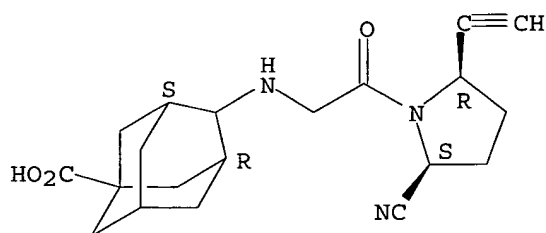
Absolute stereochemistry.



RN 866012-67-1 CAPLUS

CN Tricyclo[3.3.1.1^{3,7}]decane-1-carboxylic acid, 4-[[2-(2-cyano-5-ethynyl-1-pyrrolidinyl)-2-oxoethyl]amino]-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

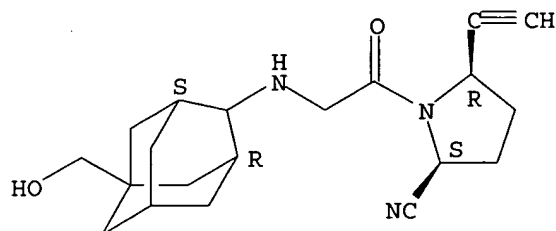


● HCl

RN 866012-68-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[5-(hydroxymethyl)tricyclo[3.3.1.13,7]dec-2-yl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 676559-46-9P 676559-52-7P 676559-53-8P
676559-55-0P 676559-60-7P 676559-62-9P
676560-43-3P 676560-88-6P 676560-89-7P
676560-95-5P 676560-96-6P 676561-18-5P
676561-23-2P 676561-24-3P 676561-25-4P
676561-77-6P 865980-50-3P 866012-69-3P

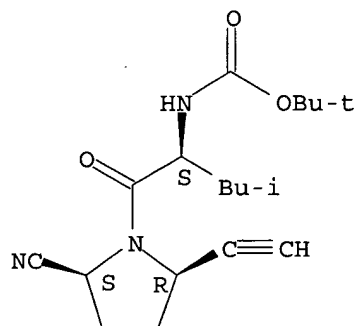
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of cyanopyrrolidine derivs. and pharmaceutical compns. thereof as inhibitors of dipeptidyl peptidase-iv (dpp-iv))

RN 676559-46-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

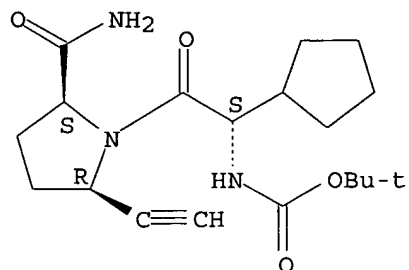
Absolute stereochemistry.



RN 676559-52-7 CAPLUS

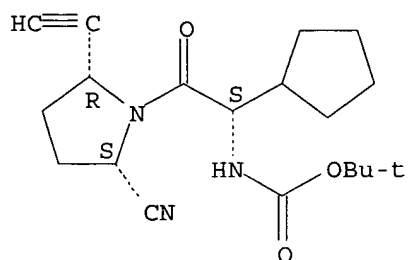
CN L-Prolinamide, (2S)-2-cyclopentyl-N-[(1,1-dimethylethoxy)carbonyl]glycyl-5-ethynyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



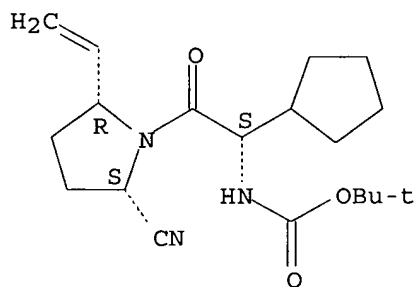
RN 676559-53-8 CAPLUS
 CN Carbamic acid, [(1S)-2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-1-cyclopentyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



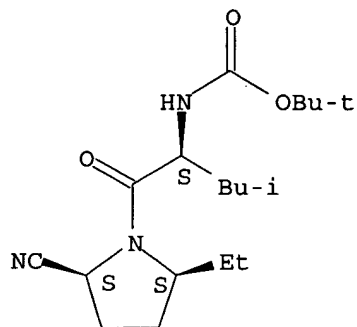
RN 676559-55-0 CAPLUS
 CN Carbamic acid, [(1S)-2-[(2S,5R)-2-cyano-5-ethenyl-1-pyrrolidinyl]-1-cyclopentyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676559-60-7 CAPLUS
 CN Carbamic acid, [(1S)-1-[[[(2S,5S)-2-cyano-5-ethyl-1-pyrrolidinyl]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

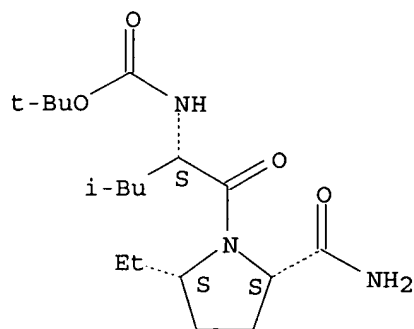
Absolute stereochemistry.



RN 676559-62-9 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl-5-ethyl-, (5S)-(9CI) (CA INDEX NAME)

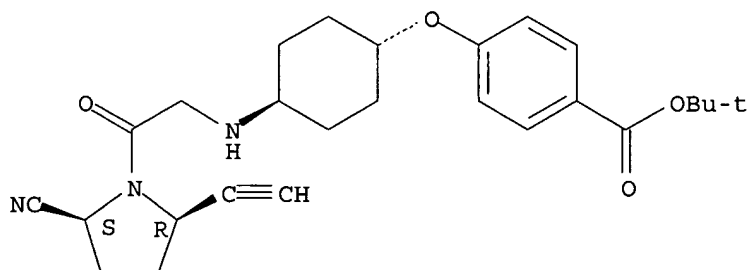
Absolute stereochemistry.



RN 676560-43-3 CAPLUS

CN Benzoic acid, 4-[[trans-4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]cyclohexyl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

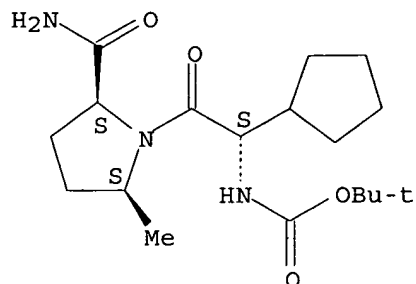
Absolute stereochemistry.



RN 676560-88-6 CAPLUS

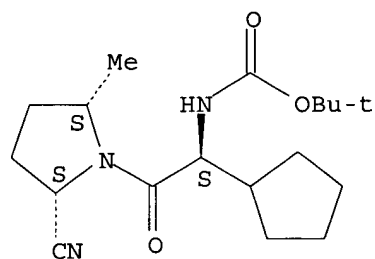
CN Carbamic acid, [(1S)-2-[(2S,5S)-2-(aminocarbonyl)-5-methyl-1-pyrrolidinyl]-1-cyclopentyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



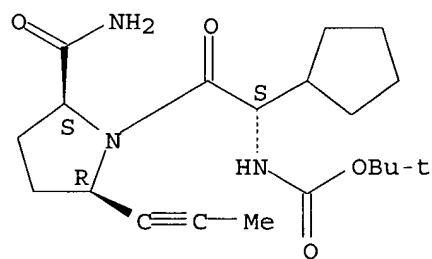
RN 676560-89-7 CAPLUS
 CN Carbamic acid, [(1S)-2-[(2S,5S)-2-cyano-5-methyl-1-pyrrolidinyl]-1-cyclopentyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



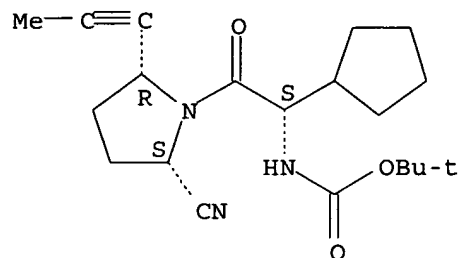
RN 676560-95-5 CAPLUS
 CN L-Prolinamide, (2S)-2-cyclopentyl-N-[(1,1-dimethylethoxy)carbonyl]glycyl-5-(1-propynyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676560-96-6 CAPLUS
 CN Carbamic acid, [(1S)-2-[(2S,5R)-2-cyano-5-(1-propynyl)-1-pyrrolidinyl]-1-cyclopentyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

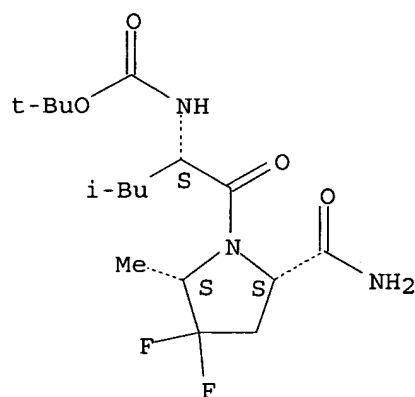
Absolute stereochemistry.



RN 676561-18-5 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl-4,4-difluoro-5-methyl-, (5S)- (9CI) (CA INDEX NAME)

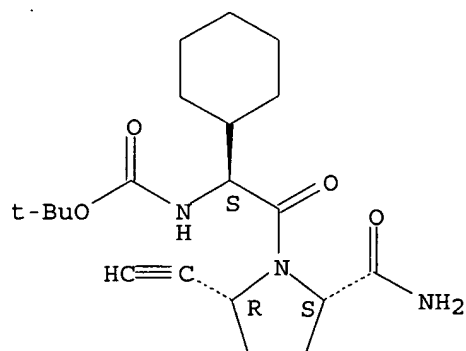
Absolute stereochemistry.



RN 676561-23-2 CAPLUS

CN L-Prolinamide, (2S)-2-cyclohexyl-N-[(1,1-dimethylethoxy)carbonyl]glycyl-5-ethynyl-, (5R)- (9CI) (CA INDEX NAME)

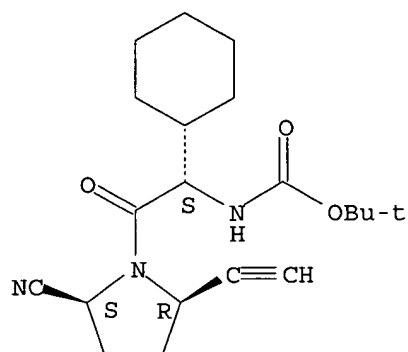
Absolute stereochemistry.



RN 676561-24-3 CAPLUS

CN Carbamic acid, [(1S)-2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-1-cyclohexyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

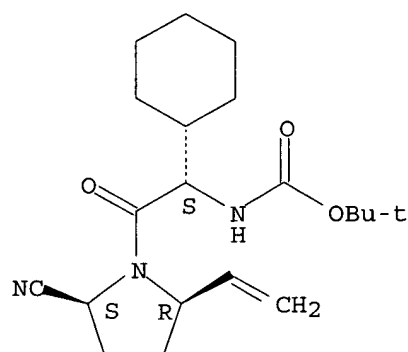
Absolute stereochemistry.



RN 676561-25-4 CAPLUS

CN Carbamic acid, [(1S)-2-[(2S,5R)-2-cyano-5-ethenyl-1-pyrrolidinyl]-1-cyclohexyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

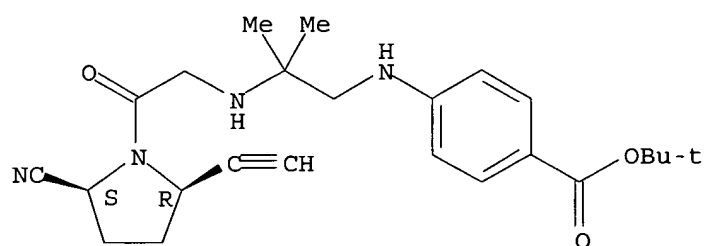
Absolute stereochemistry.



RN 676561-77-6 CAPLUS

CN Benzoic acid, 4-[[2-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-2-methylpropyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

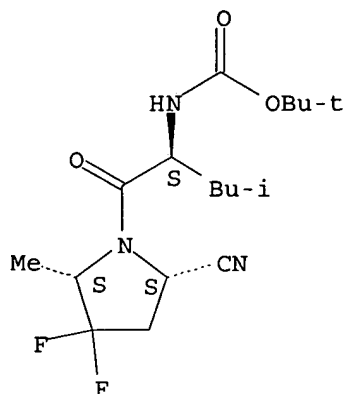
Absolute stereochemistry.



RN 865980-50-3 CAPLUS

CN Carbamic acid, [(1R)-1-[[[(2R,5R)-5-cyano-3,3-difluoro-2-methyl-1-pyrrolidinyl]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester, rel- (9CI) (CA INDEX NAME)

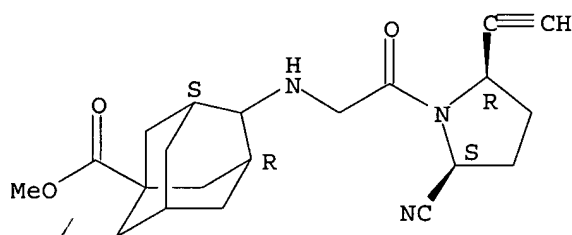
Relative stereochemistry.



RN 866012-69-3 CAPLUS

CN Tricyclo[3.3.1.1^{3,7}]decane-1-carboxylic acid, 4-[[2-(2-cyano-5-ethynyl-1-pyrrolidinyl)-2-oxoethyl]amino]-, methyl ester, monohydrochloride, (2S,5R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L51 ANSWER 4 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:984020 CAPLUS

DOCUMENT NUMBER: 143:279447

TITLE: Inhibitors of dipeptidyl peptidase IV, their preparation, and their therapeutic use

INVENTOR(S): Bachovchin, William W.; Lai, Hung-Sen; Wu, Wengen

PATENT ASSIGNEE(S): Trustees of Tufts College, USA

SOURCE: PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2005082348 | A2 | 20050909 | WO 2005-US6128 | 20050223 |

WO 2005082348

A3

20051229

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005203027

A1

20050915

US 2005-65001

20050223

PRIORITY APPLN. INFO.:

US 2004-547227P

P 20040223

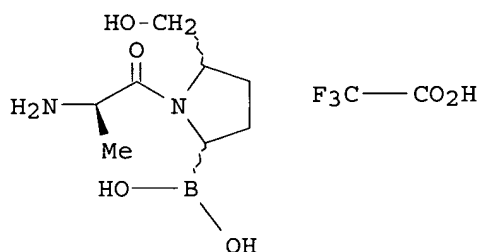
US 2004-599336P

P 20040806

OTHER SOURCE(S):

MARPAT 143:279447

GI



AB The invention relates to inhibitors of post-proline cleaving enzymes, e.g. inhibitors of dipeptidyl peptidase IV, as well as pharmaceutical compns. thereof, and methods of using such inhibitors. In particular, the inhibitors of the invention are improved over those in the prior art by selection of particular classes of sidechains in the P1 and/or P2 position of the inhibitor that contain a carboxylic acid moiety. The compds. of the invention can have a better therapeutic index, owing in part to reduced toxicity and/or improved specificity for the targeted protease. Preparation of e.g. I is included.

IT 864074-58-8P 864074-63-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(dipeptidyl peptidase IV inhibitors, and therapeutic use)

RN 864074-58-8 CAPLUS

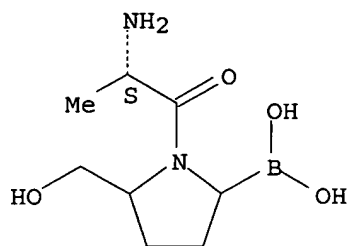
CN Boronic acid, [1-[(2S)-2-amino-1-oxopropyl]-5-(hydroxymethyl)-2-pyrrolidinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 864074-57-7

CMF C8 H17 B N2 O4

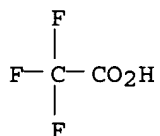
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 864074-63-5 CAPLUS

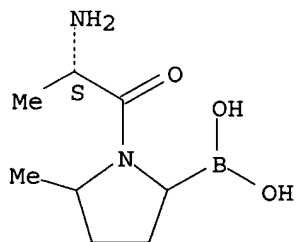
CN Boronic acid, [1-[(2S)-2-amino-1-oxopropyl]-5-methyl-2-pyrrolidinyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 864074-62-4

CMF C8 H17 B N2 O3

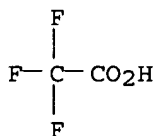
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



151 ANSWER 5 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:239012 CAPLUS

DOCUMENT NUMBER: 142:298335

TITLE: Preparation of kahalalide F analogs as antitumor agents

INVENTOR(S): Albericio Palomera, Fernando; Fernandez Donis, Ariadna; Giralt Lledo, Ernest; Gracia Cantador, Carolina; Lopez Rodriguez, Pilar; Varon Colomer, Sonia; Cuevas Marchante, Carmen; Lopez Macia, Angel; Francesch Solloso, Andres; Jiminez Garcia, Jose-Carlos; Royo Exposito, Miriam

PATENT ASSIGNEE(S): Pharma Mar, S.A.U., Spain; Ruffles, Graham Keith

SOURCE: PCT Int. Appl., 90 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2005023846 | A1 | 20050317 | WO 2004-GB3847 | 20040909 |
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| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2004270471 | A1 | 20050317 | AU 2004-270471 | 20040909 |
| EP 1664093 | A1 | 20060607 | EP 2004-768394 | 20040909 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | |
| PRIORITY APPLN. INFO.: | | | GB 2003-21066 | A 20030909 |
| | | | WO 2004-GB3847 | W 20040909 |

OTHER SOURCE(S): MARPAT 142:298335

AB The invention relates to new analogs of kahalalide F in which one or more exocyclic or cyclic amino acids has been substituted by other natural or nonnatural amino acids, masked with organic groups, or been removed or in which the terminal 5-methylhexanoyl (5-MeHex) group has been substituted by other acyl groups or been removed. Thus, [(4S)-MeHex14]-kahalalide F was prepared by the solid-phase method and assayed for cytotoxic activity against various cell lines.

IT 847834-12-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of kahalalide F analogs as antitumor agents)

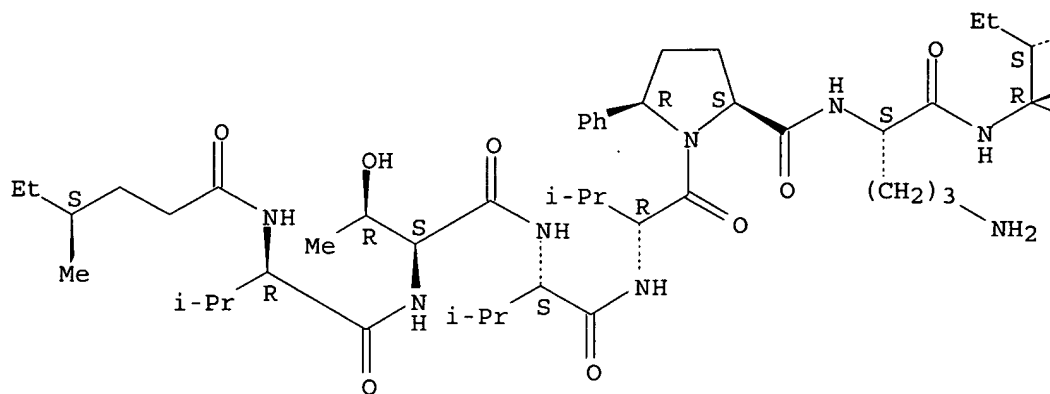
RN 847834-12-2 CAPLUS

CN Kahalalide F, 1-[N-[(4S)-4-methyl-1-oxohexyl]-D-valine]-5-[(5R)-5-phenyl-L-proline]- (9CI) (CA INDEX NAME)

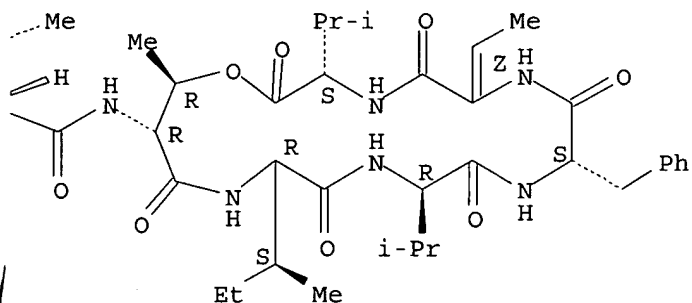
Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 6 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1127082 CAPLUS

DOCUMENT NUMBER: 142:74441

TITLE: Preparation of N-aminoacyl pyrrolidine-2-carbonitriles and related compounds as inhibitors of dipeptidyl peptidase-IV (DPP-IV) useful against type II diabetes and other disorders

INVENTOR(S): Madar, David J.; Djuric, Stevan W.; Michmerhuizen, Melissa J.; Kopecka, Hana A.; Li, Xiaofeng; Longenecker, Kenton L.; Pei, Zhonghua; Pireh, Daisy; Sham, Hing L.; Stewart, Kent D.; Szczepankiewicz, Bruce G.; Wiedeman, Paul E.; Yong, Hong

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 66 pp., Cont.-in-part of U.S. Ser. No. 659,860.

CODEN: USXXCO

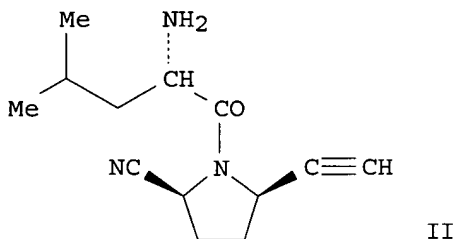
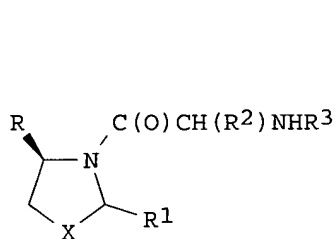
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|------------------|-----------------|-------------|
| US 2004259843 | A1 | 20041223 | US 2004-788993 | 20040227 |
| US 2004121964 | A1 | 20040624 | US 2003-659860 | 20030911 |
| US 2005215784 | A1 | 20050929 | US 2005-36258 | 20050113 |
| PRIORITY APPLN. INFO.: | | | US 2002-412084P | P 20020919 |
| | | | US 2003-659860 | A2 20030911 |
| | | | US 2004-788993 | A2 20040227 |
| OTHER SOURCE(S): | | MARPAT 142:74441 | | |
| GI | | | | |



AB The present invention relates to N-aminoacyl pyrrolidine-2-carbonitriles and related compds. (shown as I; variables defined below; e.g. II) that inhibit dipeptidyl peptidase IV (DPP-IV) and are useful for the prevention or treatment of **diabetes**, especially type II **diabetes**, as well as hyperglycemia, Syndrome X, hyperinsulinemia, obesity, atherosclerosis, and various immunomodulatory diseases (no data). Compds. I inhibit DPP-IV induced fluorescence with inhibitory consts. 0.014-7 μ M. Although the methods of preparation are not claimed, >100 example preps. are included. E.g., a 9-step synthesis of II, starting from Me (S)-(+)-2-pyrrolidone-5-carboxylate, was given. For I: X = CH₂, CHF and CF₂; R = alkylcarbonyl, arylcarbonyl, cyano, heterocyclylcarbonyl, R₄R₅NC(O)-, B(OR₆)₂, 1,3,2-dioxaborolane and 4,4,5,5-tetramethyl-1,3,2-dioxaborolane; R₁ = alkoxyalkyl, alkyl, alkylcarbonyl, alkenyl, alkynyl, allenyl, arylalkyl, cycloalkyl, cycloalkylalkyl, cyano, haloalkyl, haloalkenyl, heterocyclylalkyl, and hydroxyalkyl. R₂ and R₃ = H, alkoxyalkyl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocycle, heterocyclealkyl, hydroxyalkyl; or R₂ and R₃ taken together with the atoms to which they are attached form a mono or bicyclic heterocycle 2-indolinyl, 2-indolyl, 3-isoquinolinyl, 2-piperazinyl, 2-piperidinyl, 2-pyrrolidinyl, 2-pyrrolyl, 2-pyridinyl, 2-quinolinyl, 2-tetrahydroquinolinyl, and 3-tetrahydroisoquinolinyl, wherein said heterocycle may be substituted with 0-3 alkenyl, alkoxy, alkoxyalkyl, alkoxy carbonyl, alkoxy carbonylalkyl, alkyl, alkylcarbonyl, alkylcarbonylalkyl, alkylcarbonyloxy, alkylsulfonyl, alkylthio, alkynyl, aryl, arylalkoxy, arylalkyl, arylcarbonyl, aryloxy, carboxy, carboxyalkyl, cyano, cyanoalkyl, formyl, halogen, haloalkyl, hydroxy, hydroxyalkyl, mercapto, nitro, Ph, R₄R₅N-, R₄R₅NC(O)-, and R₄R₅NCNS(O)₂-. R₄, R₅ and R₆ = H, alkyl, and arylalkyl; R_A and R_B = alkyl, alkylcarbonyl, alkoxy carbonyl, alkylsulfonyl; or R_A and R_B taken together with the N to which they are attached form a ring piperidine, piperazine and morpholine; and R_C and R_D = H and alkyl.

IT 676560-63-7P 676561-27-6P 676561-65-2P
676561-72-1P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

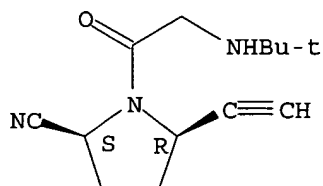
(Preparation); RACT (Reactant or reagent); USES (Uses)

(drug candidate; preparation of N-aminoacyl pyrrolidine-2-carbonitriles and related compds. as inhibitors of dipeptidyl peptidase-IV useful against type II **diabetes** and other disorders)

RN 676560-63-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(1,1-dimethylethyl)amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

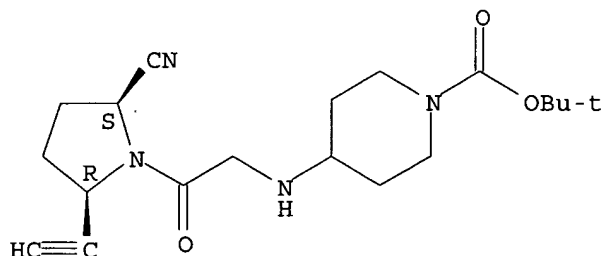
Absolute stereochemistry.



RN 676561-27-6 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

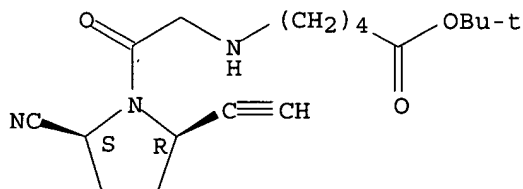
Absolute stereochemistry.



RN 676561-65-2 CAPLUS

CN Pentanoic acid, 5-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

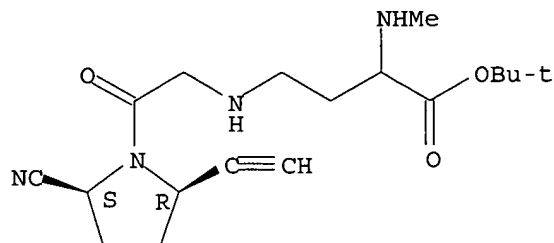
Absolute stereochemistry.



RN 676561-72-1 CAPLUS

CN Butanoic acid, 4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-2-(methylamino)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 676559-41-4P 676559-47-0P 676559-48-1P
 676559-54-9P 676559-56-1P 676559-57-2P
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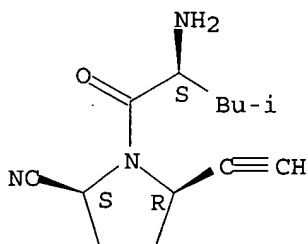
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of N-aminoacyl pyrrolidine-2-carbonitriles and related compds. as inhibitors of dipeptidyl peptidase-IV useful against type II **diabetes** and other disorders)

RN 676559-41-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-5-ethynyl-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

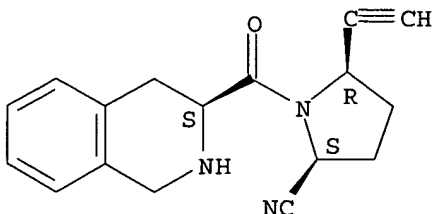


● HCl

RN 676559-47-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(3S)-1,2,3,4-tetrahydro-3-isoquinolinyl]carbonyl]-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

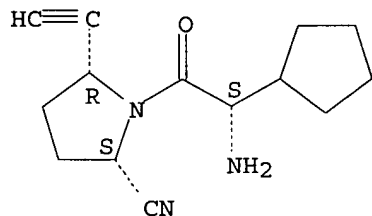


● HCl

RN 676559-48-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclopentylacetyl]-5-ethynyl-,
monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

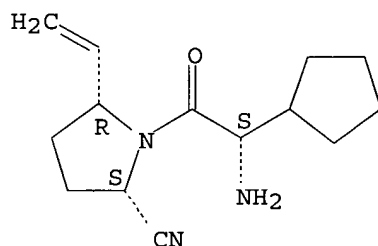


● HCl

RN 676559-54-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclopentylacetyl]-5-ethenyl-,
monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

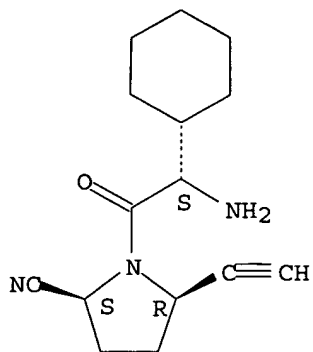


● HCl

RN 676559-56-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclohexylacetyl]-5-ethynyl-,
monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

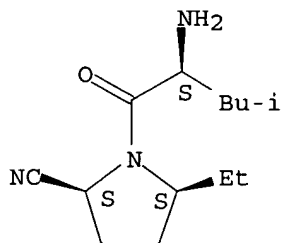


● HCl

RN 676559-57-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-5-ethyl-, (2S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676559-58-3 CAPLUS

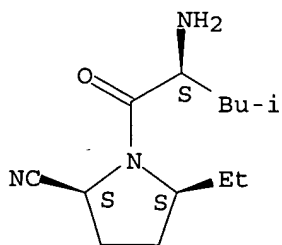
CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-5-ethyl-, (2S,5S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 676559-57-2

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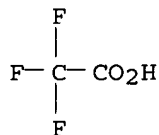
Absolute stereochemistry.



CM 2

CRN 76-05-1

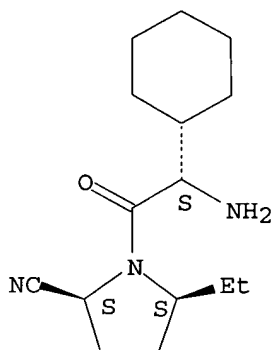
CMF C2 H F3 O2



RN 676559-63-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclohexylacetyl]-5-ethyl-,
(2S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676559-64-1 CAPLUS

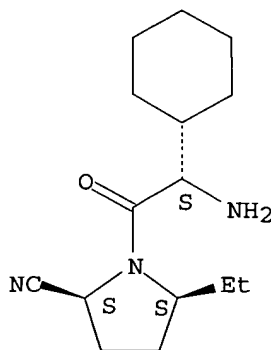
CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclohexylacetyl]-5-ethyl-,
(2S,5S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 676559-63-0

CMF C15 H25 N3 O

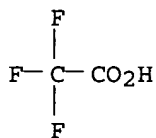
Absolute stereochemistry.



CM 2

CRN 76-05-1

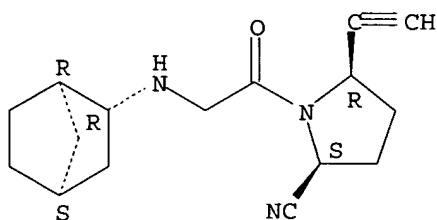
CMF C2 H F3 O2



RN 676559-65-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(1R,2R,4S)-bicyclo[2.2.1]hept-2-ylamino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

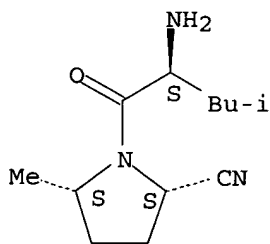
Absolute stereochemistry.



RN 676559-70-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

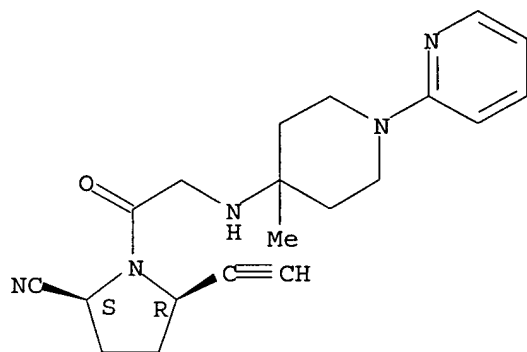
Absolute stereochemistry.



RN 676559-71-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-(2-pyridinyl)-4-piperidinylamino]acetyl]-, hydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

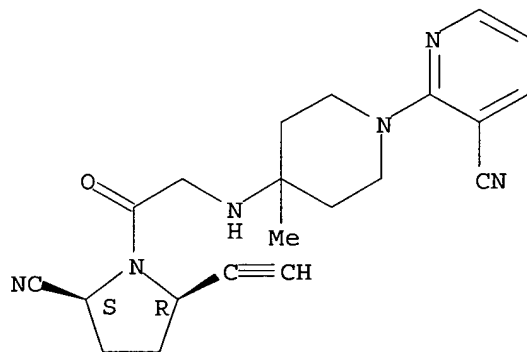


●x HCl

RN 676559-73-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(3-cyano-2-pyridinyl)-4-methyl-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

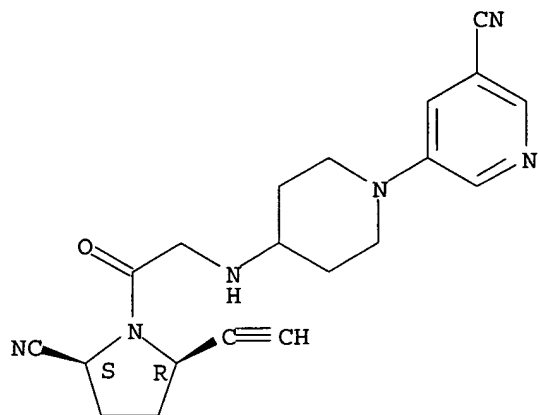
Absolute stereochemistry.



RN 676559-76-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-3-pyridinyl)-4-piperidinyl]amino]acetyl]-5-ethynyl-, hydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

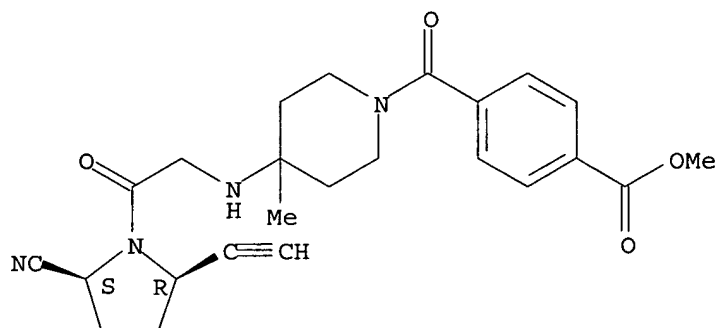


●x HCl

RN 676559-80-1 CAPLUS

CN Benzoic acid, 4-[[4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-4-methyl-1-piperidiny]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

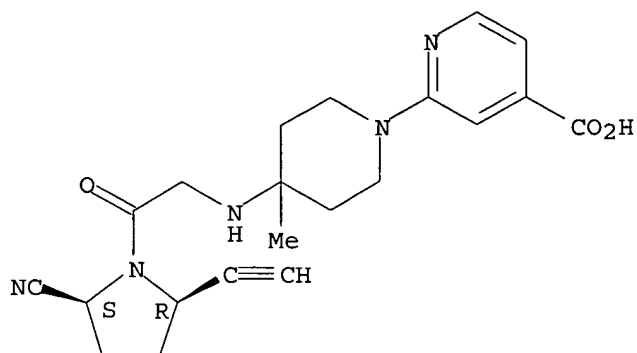
Absolute stereochemistry.



RN 676559-83-4 CAPLUS

CN 4-Pyridinecarboxylic acid, 2-[4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-4-methyl-1-piperidiny]- (9CI) (CA INDEX NAME)

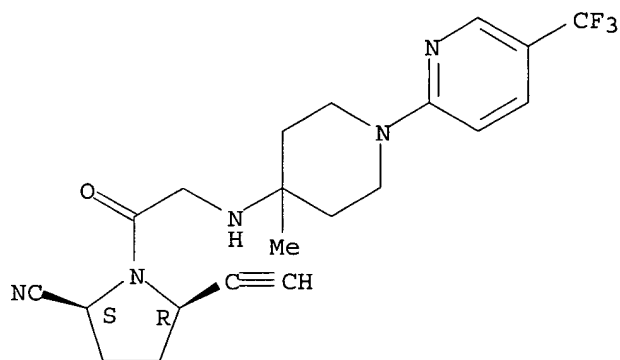
Absolute stereochemistry.



RN 676559-84-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[5-(trifluoromethyl)-2-pyridinyl]-4-piperidinyl]amino]acetyl]-, hydrochloride, (2S,5R)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

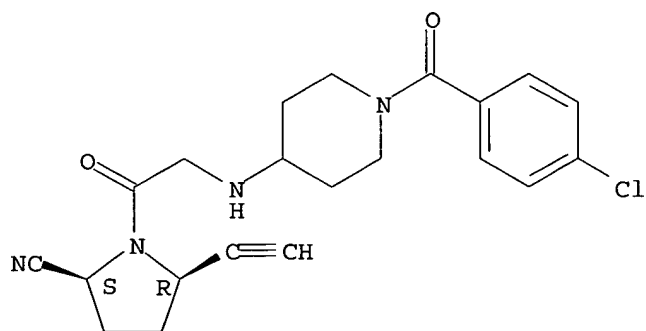


●x HCl

RN 676559-86-7 CAPLUS

CN 4-Piperidinamine, 1-(4-chlorobenzoyl)-N-[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

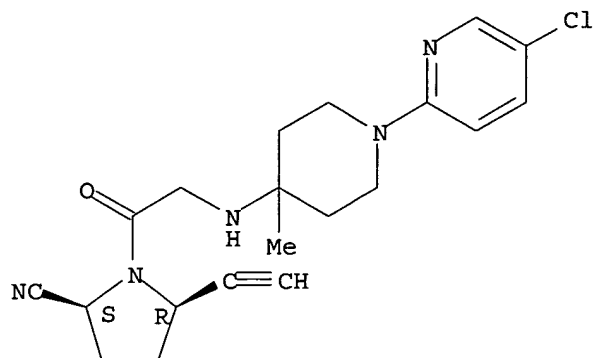
Absolute stereochemistry.



RN 676559-88-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-chloro-2-pyridinyl)-4-methyl-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676559-89-0 CAPLUS

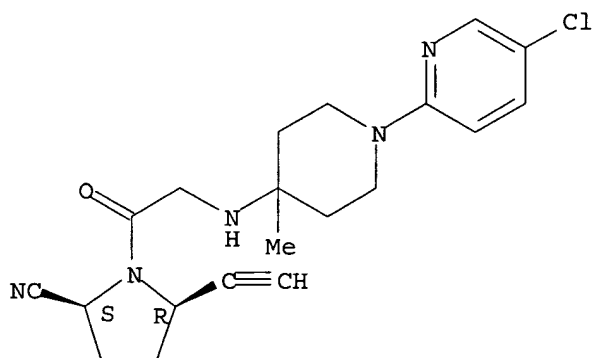
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-chloro-2-pyridinyl)-4-methyl-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 676559-88-9

CMF C20 H24 Cl N5 O

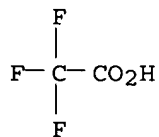
Absolute stereochemistry.



CM 2

CRN 76-05-1

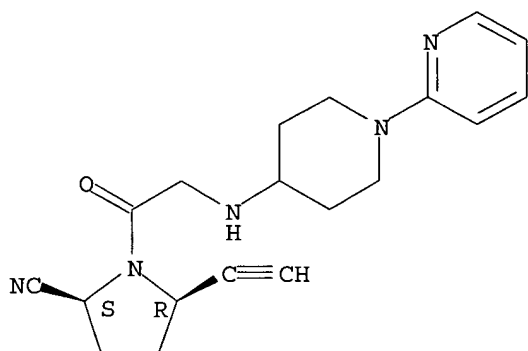
CMF C2 H F3 O2



RN 676559-91-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1-(2-pyridinyl)-4-piperidinyl]aminolacetyl]-, hydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

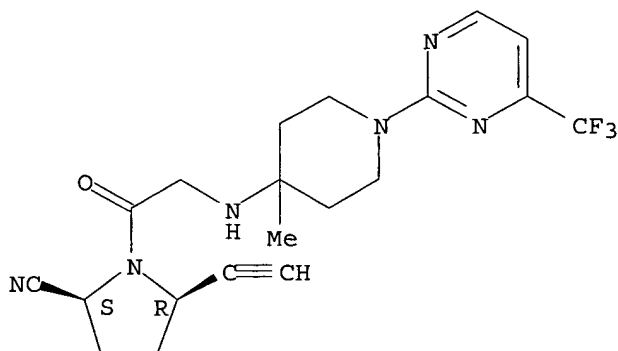


●_x HCl

RN 676559-92-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[4-(trifluoromethyl)-2-pyrimidinyl]-4-piperidinyl]aminolacetyl]-, hydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

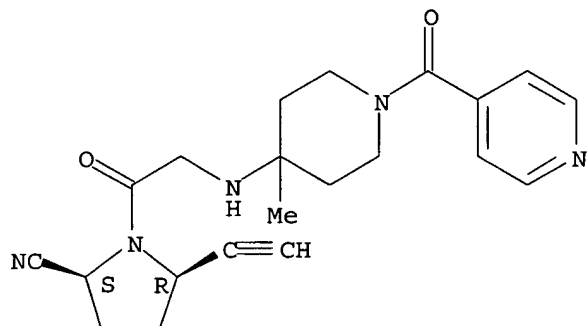


●_x HCl

RN 676559-95-8 CAPLUS

CN 4-Piperidinamine, N-[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]-4-methyl-1-(4-pyridinylcarbonyl)-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

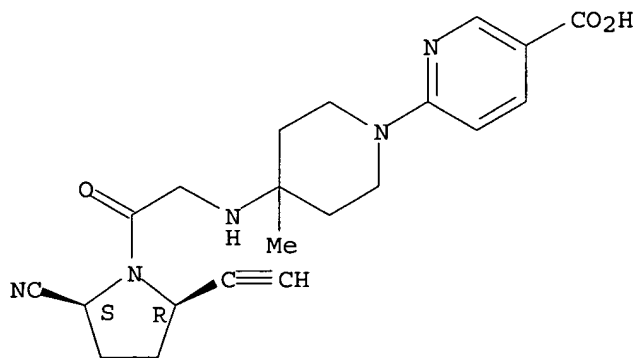


● x HCl

RN 676559-99-2 CAPLUS

CN 3-Pyridinecarboxylic acid, 6-[4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-4-methyl-1-piperidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676560-00-2 CAPLUS

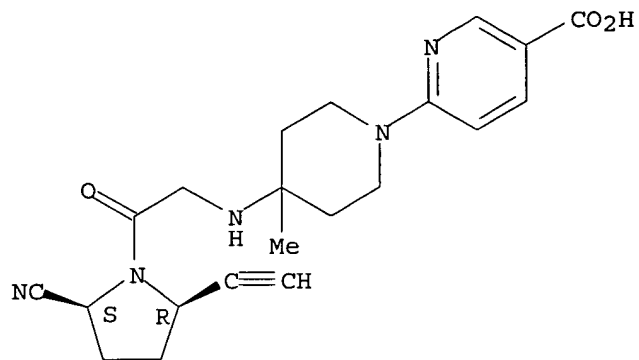
CN 3-Pyridinecarboxylic acid, 6-[4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-4-methyl-1-piperidinyl]-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 676559-99-2

CMF C21 H25 N5 O3

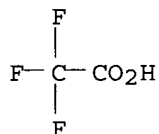
Absolute stereochemistry.



CM 2

CRN 76-05-1

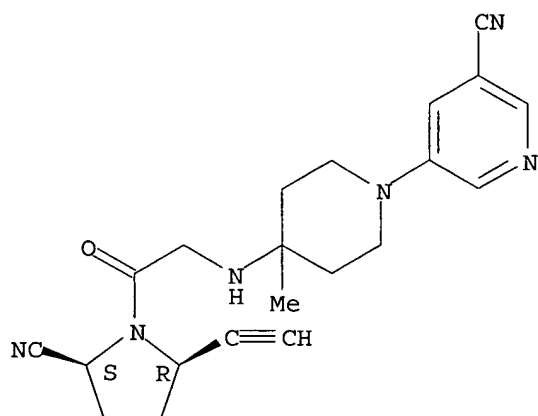
CMF C2 H F3 O2



RN 676560-04-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-3-pyridinyl)-4-methyl-4-piperidinyl]amino]acetyl]-5-ethynyl-, hydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



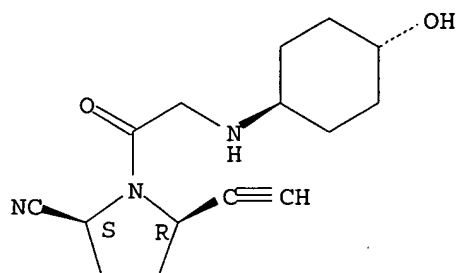
●x HCl

RN 676560-07-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(trans-4-

hydroxycyclohexyl)amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

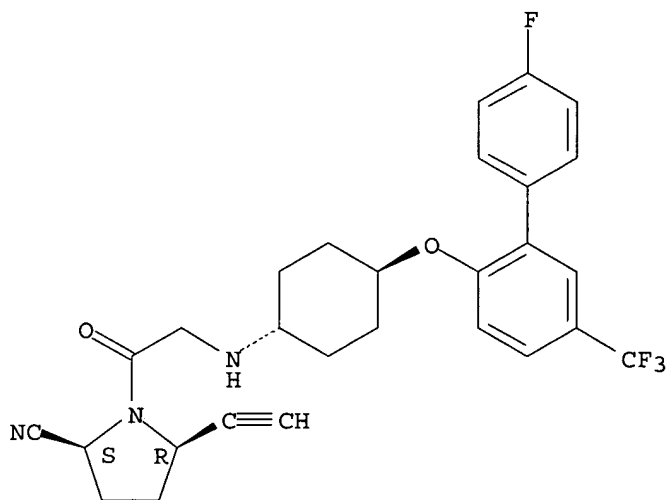
Absolute stereochemistry.



RN 676560-08-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[4'-fluoro-5-(trifluoromethyl)[1,1'-biphenyl]-2-yl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

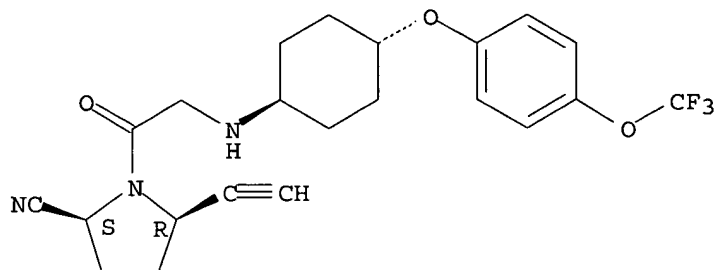
Absolute stereochemistry.



RN 676560-13-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[4-(trifluoromethoxy)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

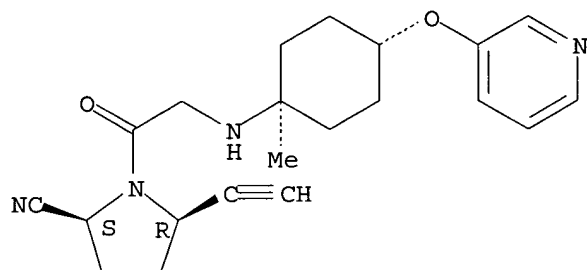
Absolute stereochemistry.



RN 676560-20-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-1-methyl-4-(3-pyridinyloxy)cyclohexyl]amino]acetyl]-, hydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

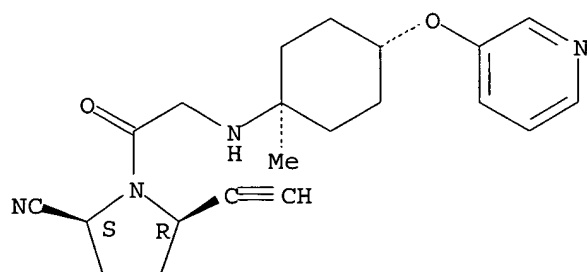


● x HCl

RN 676560-22-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-1-methyl-4-(3-pyridinyloxy)cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

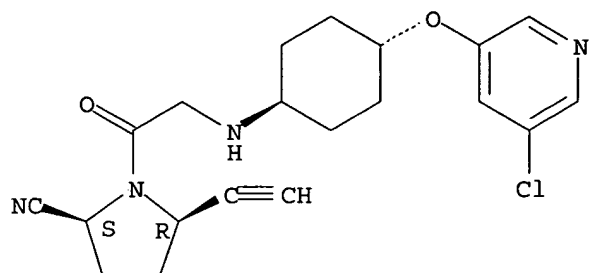
Absolute stereochemistry.



RN 676560-23-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(5-chloro-3-pyridinyl)oxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

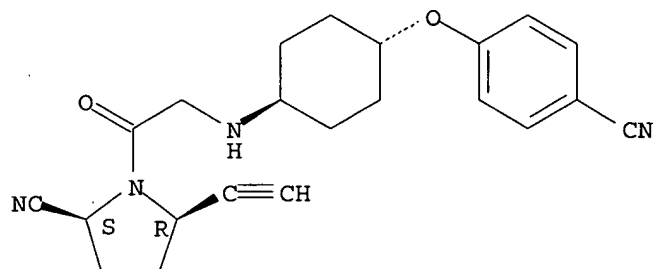
Absolute stereochemistry.



RN 676560-25-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(4-cyanophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

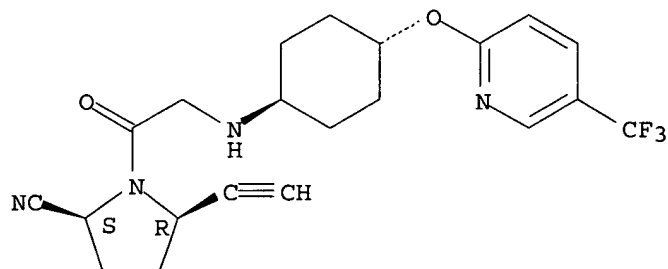
Absolute stereochemistry.



RN 676560-27-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[5-(trifluoromethyl)-2-pyridinyl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

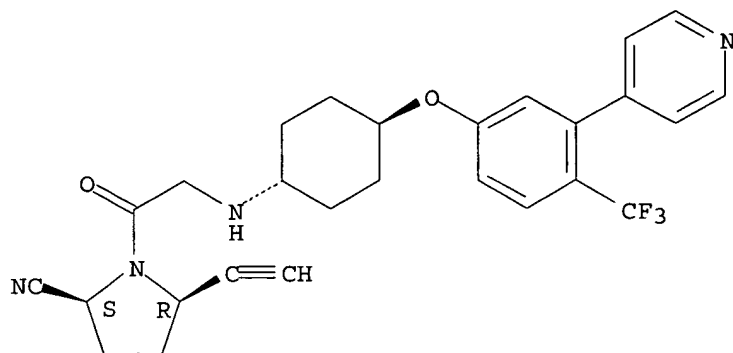
Absolute stereochemistry.



RN 676560-29-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[3-(4-pyridinyl)-4-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

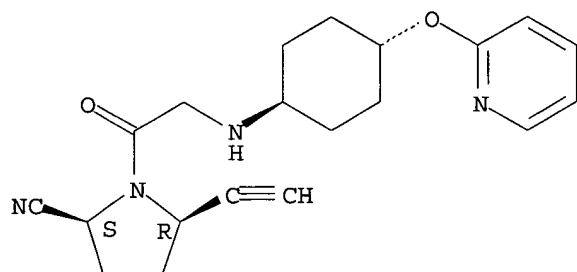
Absolute stereochemistry.



RN 676560-34-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-(2-pyridinyloxy)cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

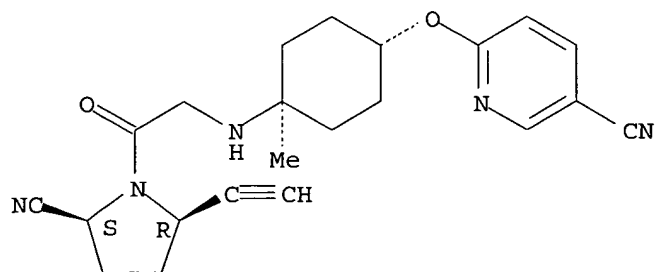
Absolute stereochemistry.



RN 676560-35-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(5-cyano-2-pyridinyl)oxy]-1-methylcyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

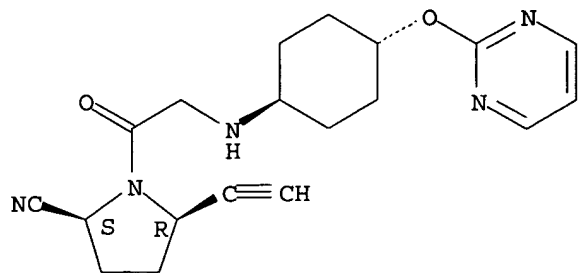
Absolute stereochemistry.



RN 676560-36-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-(2-pyrimidinyl)oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

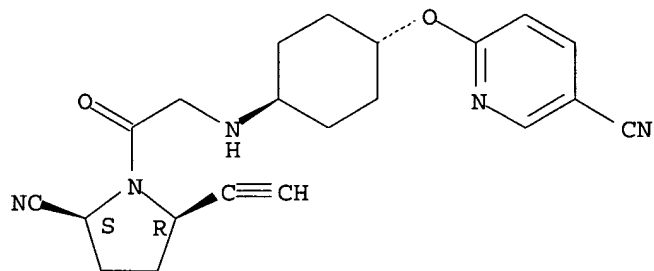
Absolute stereochemistry.



RN 676560-37-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(5-cyano-2-pyridinyl)oxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

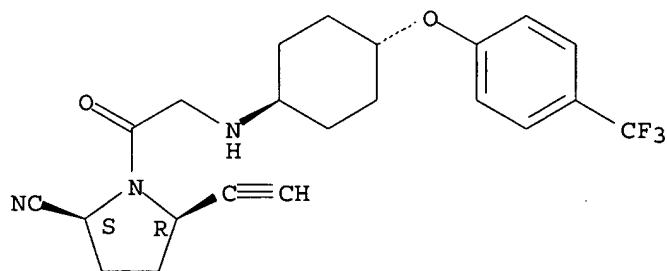
Absolute stereochemistry.



RN 676560-39-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[4-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

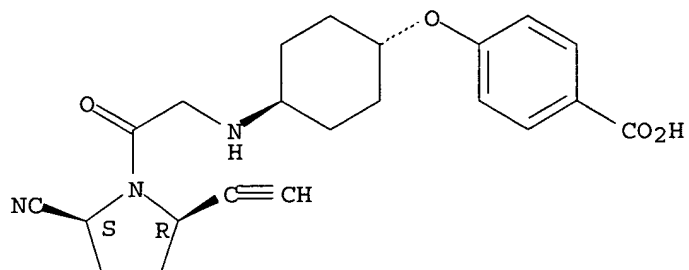
Absolute stereochemistry.



RN 676560-41-1 CAPLUS

CN Benzoic acid, 4-[[[trans-4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]cyclohexyl]oxy]- (9CI) (CA INDEX NAME)

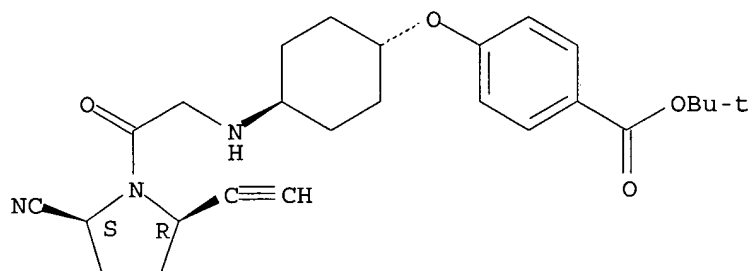
Absolute stereochemistry.



RN 676560-43-3 CAPLUS

CN Benzoic acid, 4-[[[trans-4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]cyclohexyl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

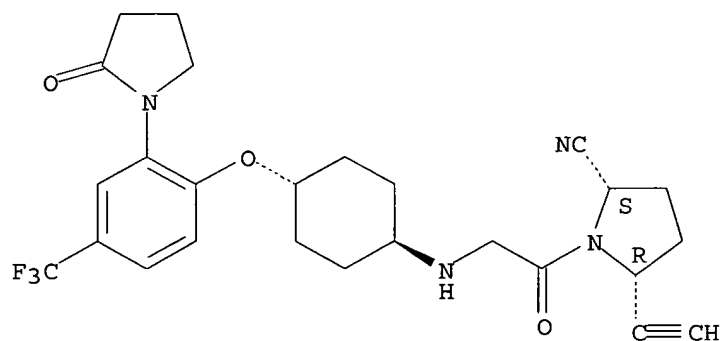
Absolute stereochemistry.



RN 676560-44-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[2-(2-oxo-1-pyrrolidinyl)-4-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

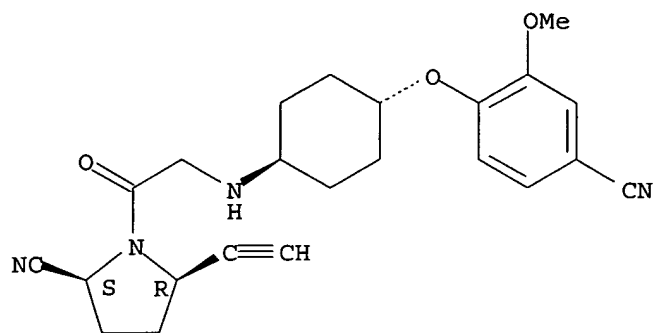
Absolute stereochemistry.



RN 676560-47-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(4-cyano-2-methoxyphenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

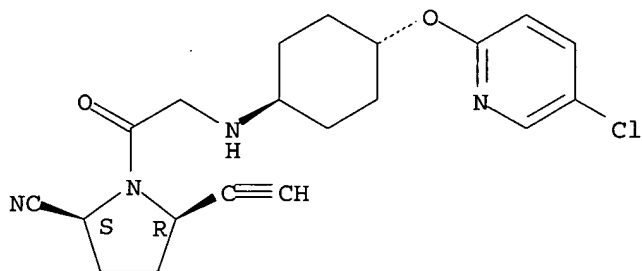
Absolute stereochemistry.



RN 676560-50-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(5-chloro-2-pyridinyl)oxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

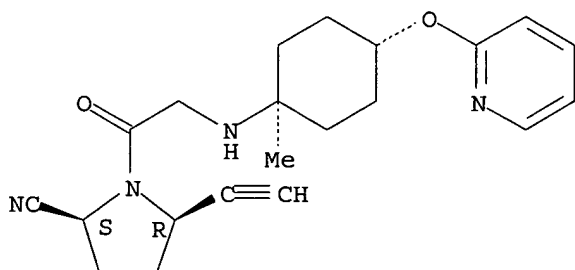
Absolute stereochemistry.



RN 676560-52-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-1-methyl-4-(2-pyridinyloxy)cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

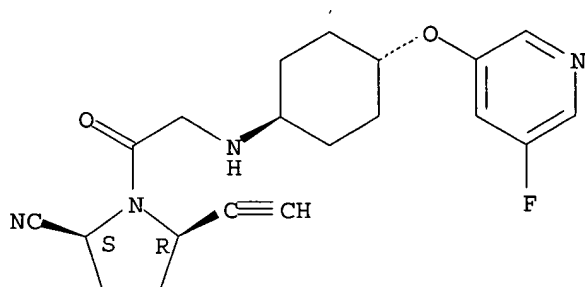
Absolute stereochemistry.



RN 676560-54-6 CAPLUS

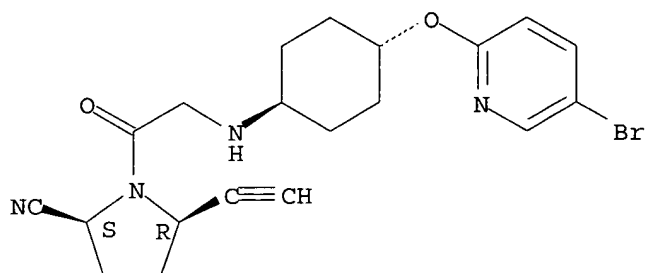
CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[(5-fluoro-3-pyridinyl)oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



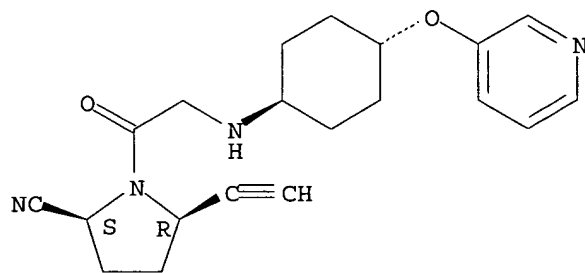
RN 676560-56-8 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(5-bromo-2-pyridinyl)oxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



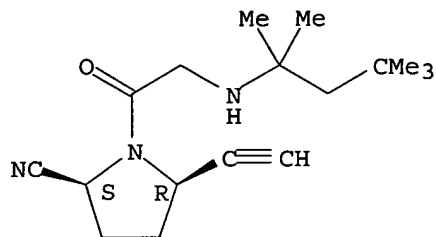
RN 676560-58-0 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-(3-pyridinyloxy)cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676560-60-4 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-(3-pyridinyloxy)cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

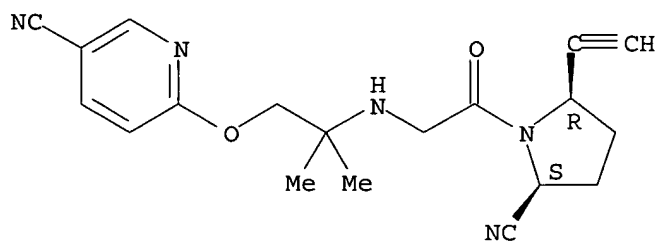
Absolute stereochemistry.



RN 676560-61-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(5-cyano-2-pyridinyl)oxy]-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

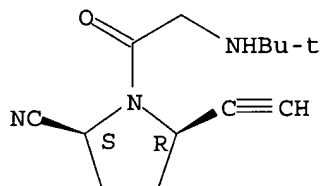
Absolute stereochemistry.



RN 676560-64-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

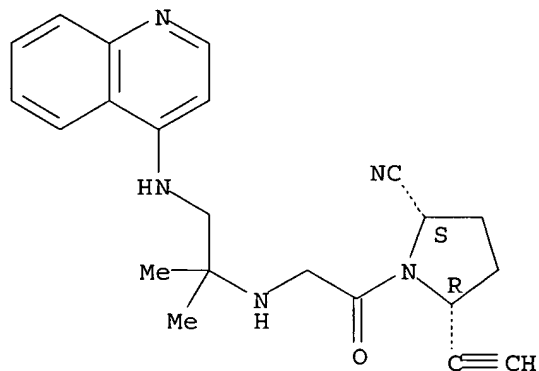


● HCl

RN 676560-65-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1,1-dimethyl-2-(4-quinolinylamino)ethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

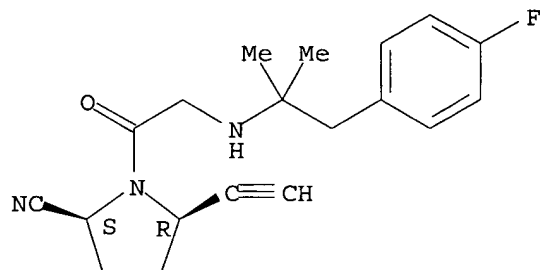
Absolute stereochemistry.



RN 676560-66-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[2-(4-fluorophenyl)-1,1-dimethylethyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

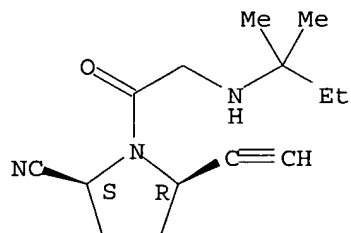
Absolute stereochemistry.



RN 676560-67-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(1,1-dimethylpropyl)amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

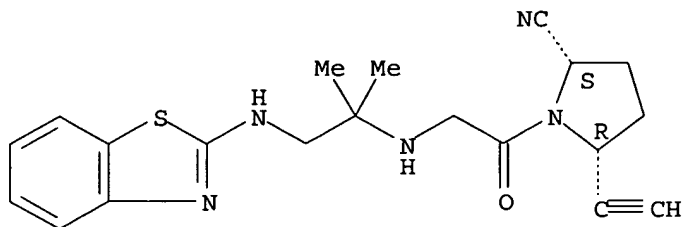
Absolute stereochemistry.



RN 676560-68-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-(2-benzothiazolylamino)-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

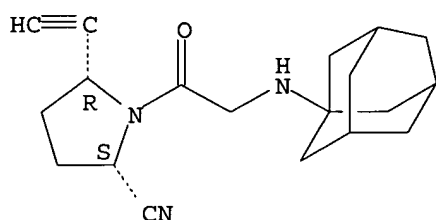
Absolute stereochemistry.



RN 676560-69-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[(tricyclo[3.3.1.1^{3,7}]dec-1-ylamino)acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

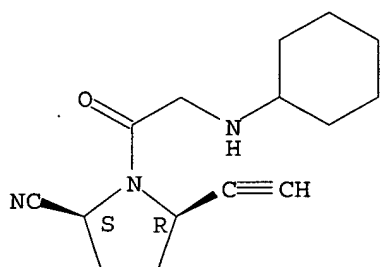
Absolute stereochemistry.



RN 676560-70-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclohexylamino)acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

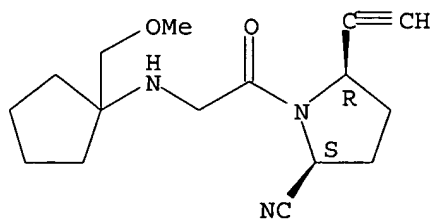
Absolute stereochemistry.



RN 676560-71-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1-(methoxymethyl)cyclopentyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

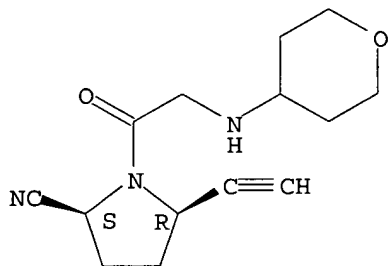
Absolute stereochemistry.



RN 676560-75-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(tetrahydro-2H-pyran-4-yl)amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

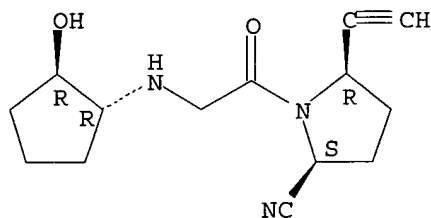
Absolute stereochemistry.



RN 676560-76-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(1R,2R)-2-hydroxycyclopentyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

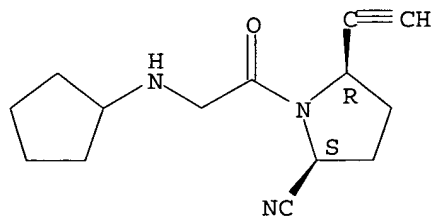
Absolute stereochemistry.



RN 676560-77-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclopentylamino)acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

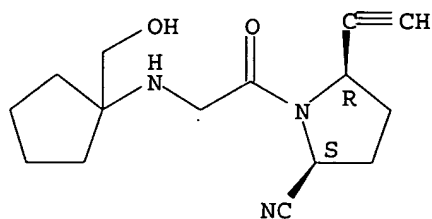
Absolute stereochemistry.



RN 676560-79-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1-(hydroxymethyl)cyclopentyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

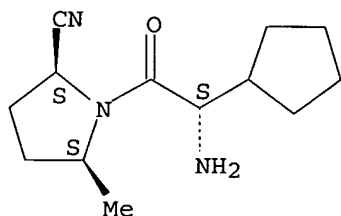
Absolute stereochemistry.



RN 676560-81-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclopentylacetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

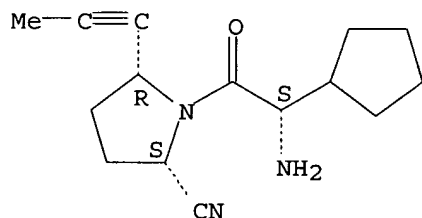
Absolute stereochemistry.



RN 676560-90-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclopentylacetyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

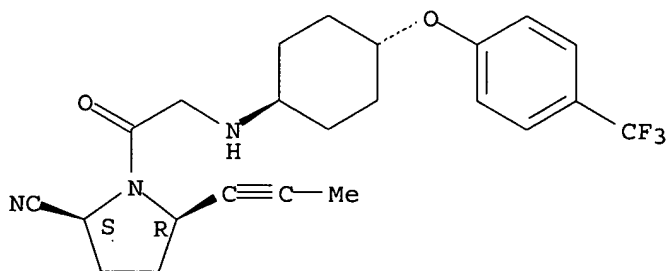
Absolute stereochemistry.



RN 676560-97-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-(1-propynyl)-1-[[[trans-4-[4-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

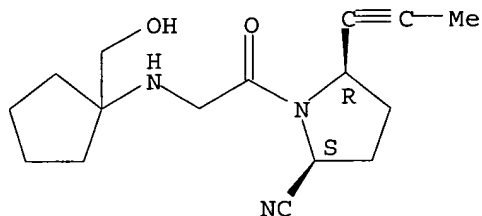
Absolute stereochemistry.



RN 676560-99-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(hydroxymethyl)cyclopentyl]amino]acetyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

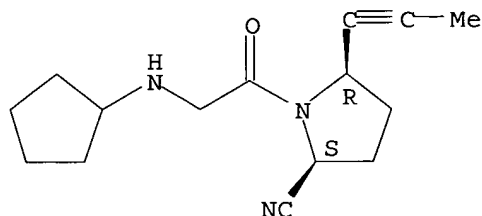
Absolute stereochemistry.



RN 676561-00-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclopentylamino)acetyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

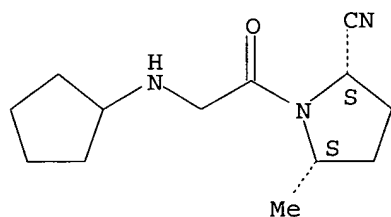
Absolute stereochemistry.



RN 676561-04-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclopentylamino)acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

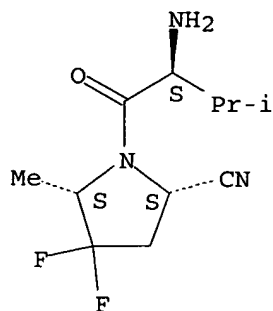
Absolute stereochemistry.



RN 676561-07-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3-methyl-1-oxobutyl]-4,4-difluoro-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

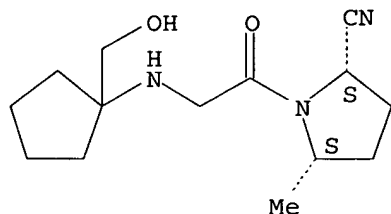
Absolute stereochemistry.



RN 676561-09-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(hydroxymethyl)cyclopentyl]amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

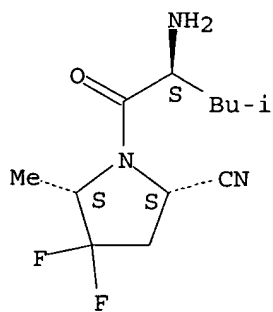
Absolute stereochemistry.



RN 676561-10-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-4,4-difluoro-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

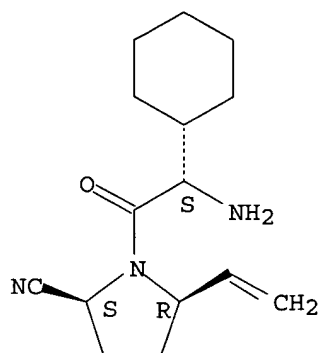
Absolute stereochemistry.



RN 676561-20-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclohexylacetyl]-5-ethenyl-, (2S,5R)- (9CI) (CA INDEX NAME)

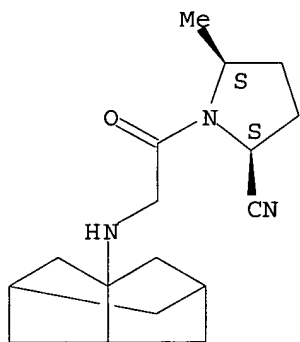
Absolute stereochemistry.



RN 676561-26-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(hexahydro-2,5-methanopentalen-3a(1H)-yl)amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

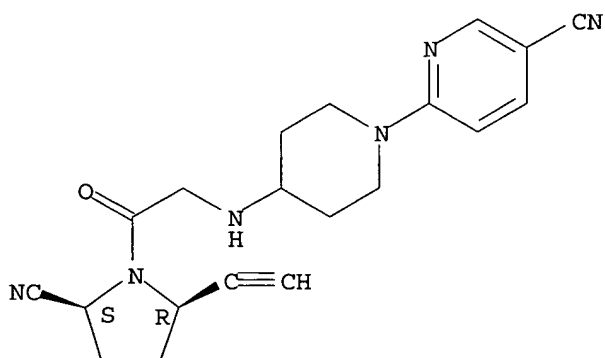
Absolute stereochemistry.



RN 676561-28-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-2-pyridinyl)-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

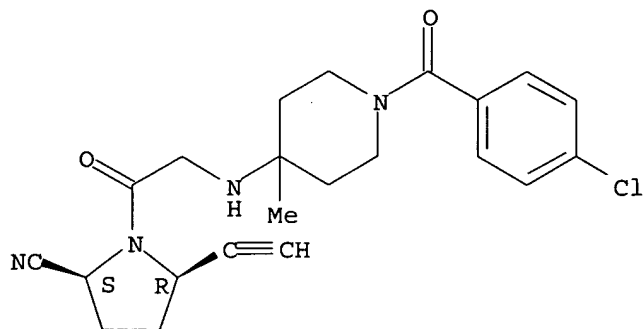
Absolute stereochemistry.



RN 676561-29-8 CAPLUS

CN 4-Piperidinamine, 1-(4-chlorobenzoyl)-N-[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]-4-methyl-, (9CI) (CA INDEX NAME)

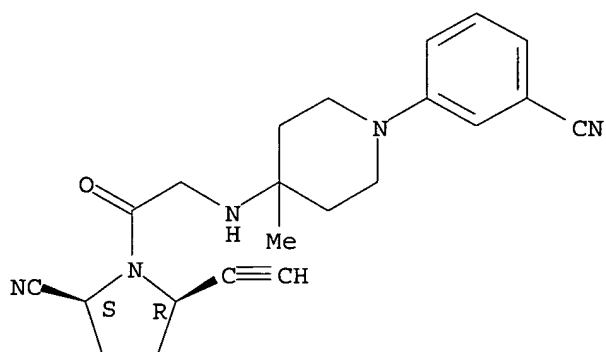
Absolute stereochemistry.



RN 676561-30-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(3-cyanophenyl)-4-methyl-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

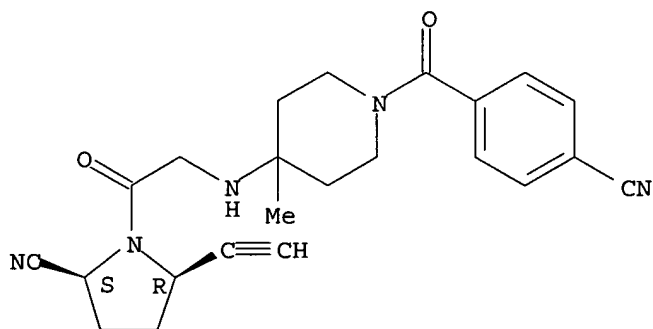
Absolute stereochemistry.



RN 676561-31-2 CAPLUS

CN 4-Piperidinamine, 1-(4-cyanobenzoyl)-N-[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]-4-methyl- (9CI) (CA INDEX NAME)

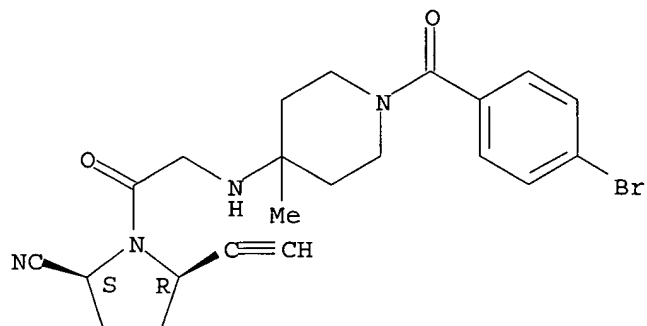
Absolute stereochemistry.



RN 676561-32-3 CAPLUS

CN 4-Piperidinamine, 1-(4-bromobenzoyl)-N-[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]-4-methyl- (9CI) (CA INDEX NAME)

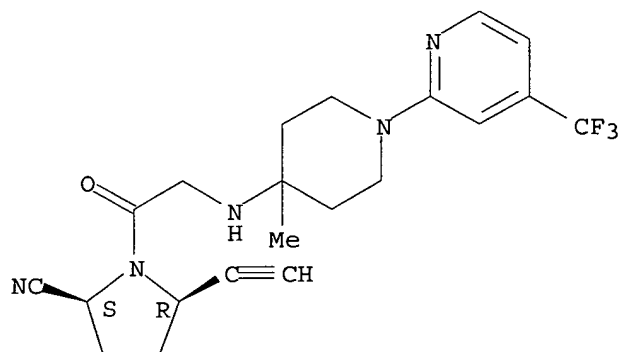
Absolute stereochemistry.



RN 676561-33-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[4-(trifluoromethyl)-2-pyridinyl]-4-piperidinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

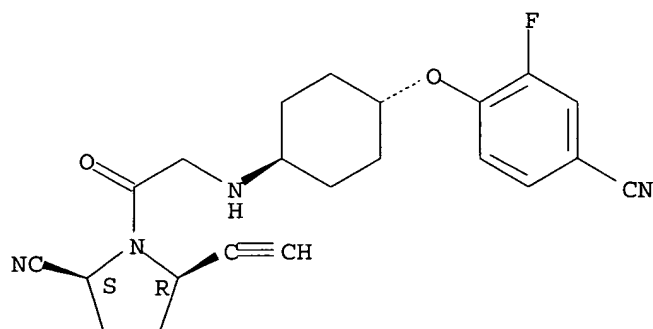
Absolute stereochemistry.



RN 676561-34-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(4-cyano-2-fluorophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

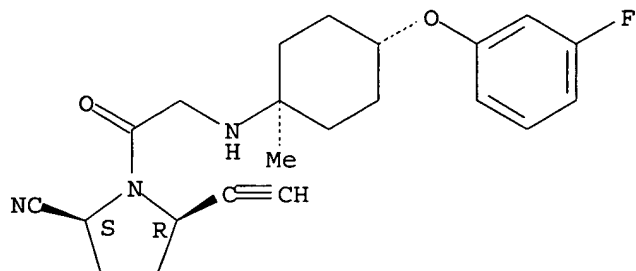
Absolute stereochemistry.



RN 676561-35-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-(3-fluorophenoxy)-1-methylcyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

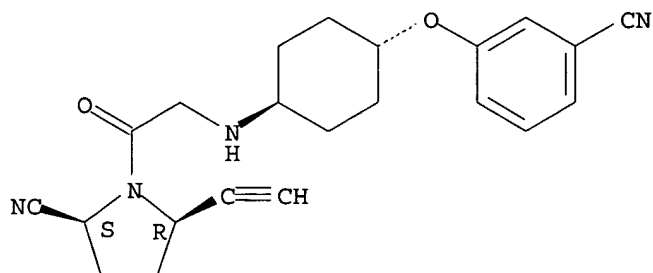
Absolute stereochemistry.



RN 676561-36-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(3-cyanophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

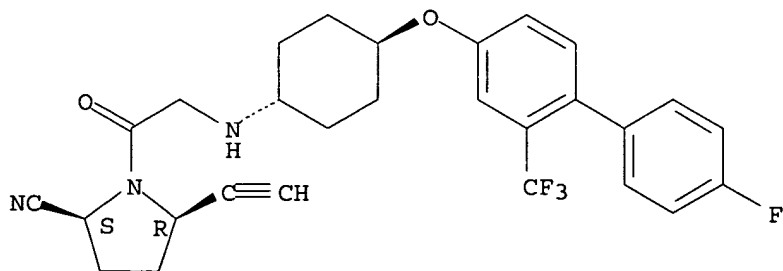
Absolute stereochemistry.



RN 676561-37-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[4'-fluoro-2-(trifluoromethyl)[1,1'-biphenyl]-4-yl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

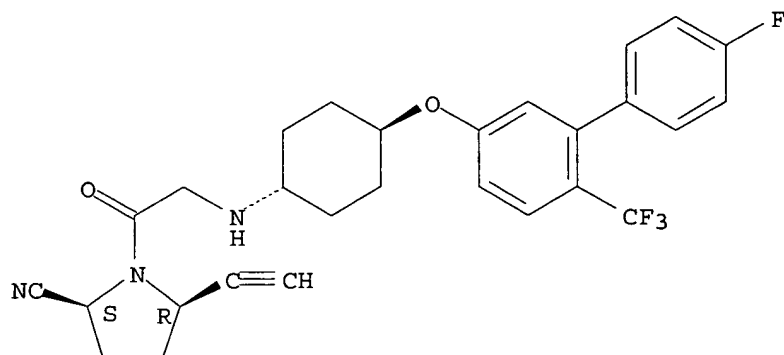
Absolute stereochemistry.



RN 676561-38-9 CAPLUS

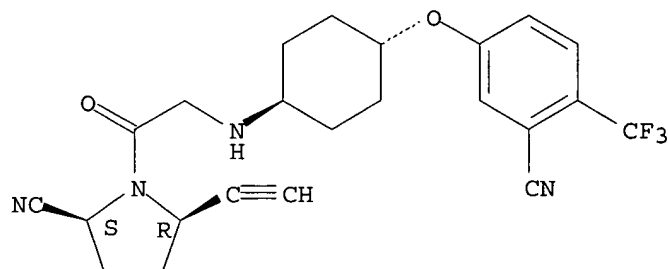
CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[4'-fluoro-6-(trifluoromethyl)[1,1'-biphenyl]-3-yl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



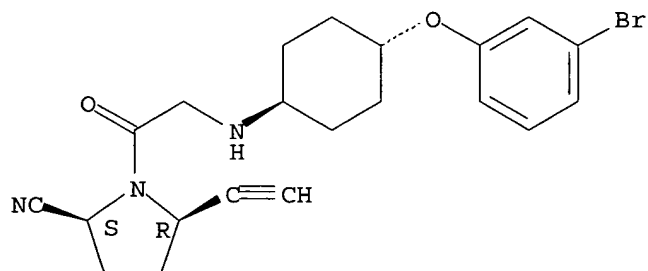
RN 676561-39-0 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[3-cyano-4-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



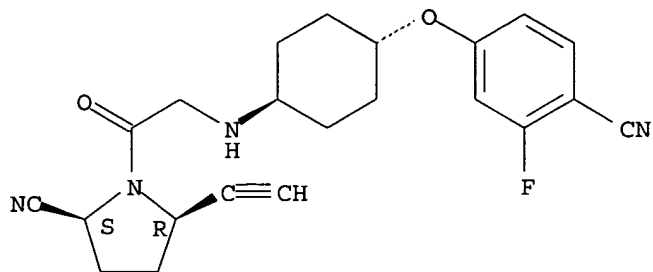
RN 676561-40-3 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(3-bromophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676561-41-4 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(4-cyano-3-fluorophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

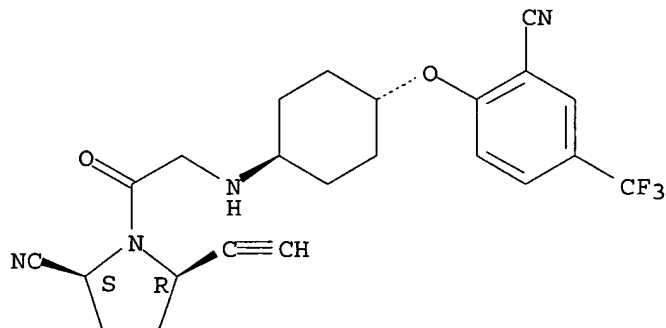
Absolute stereochemistry.



RN 676561-42-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[2-cyano-4-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

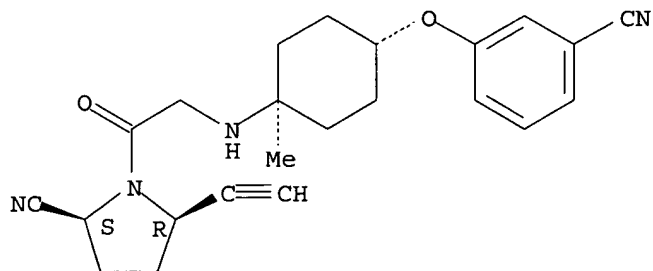
Absolute stereochemistry.



RN 676561-43-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(3-cyanophenoxy)-1-methylcyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

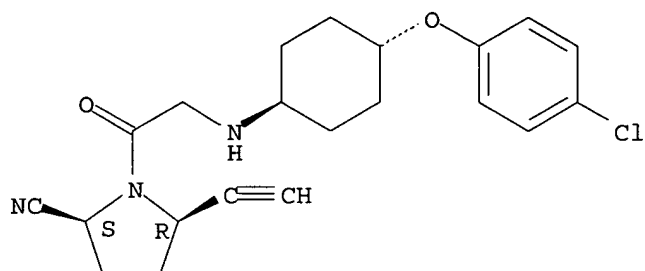
Absolute stereochemistry.



RN 676561-44-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(4-chlorophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

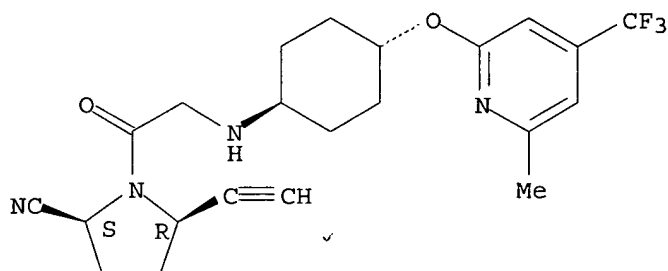
Absolute stereochemistry.



RN 676561-45-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[6-methyl-4-(trifluoromethyl)-2-pyridinyl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)-(9CI) (CA INDEX NAME)

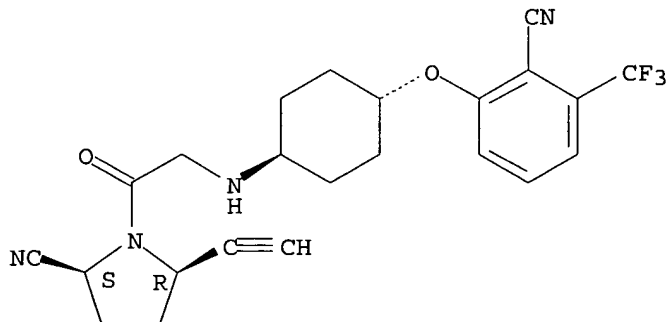
Absolute stereochemistry.



RN 676561-46-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[2-cyano-3-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)-(9CI) (CA INDEX NAME)

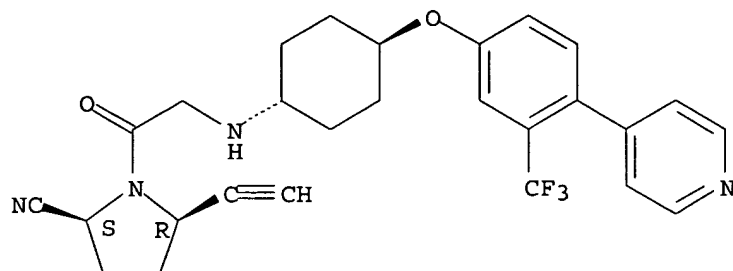
Absolute stereochemistry.



RN 676561-47-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[4-(4-pyridinyl)-3-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)-(9CI) (CA INDEX NAME)

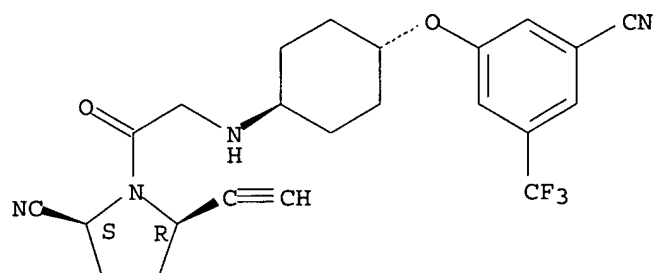
Absolute stereochemistry.



RN 676561-48-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[3-cyano-5-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)-(9CI) (CA INDEX NAME)

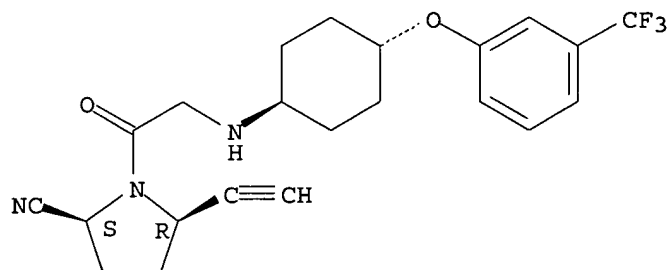
Absolute stereochemistry.



RN 676561-49-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[3-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)-(9CI) (CA INDEX NAME)

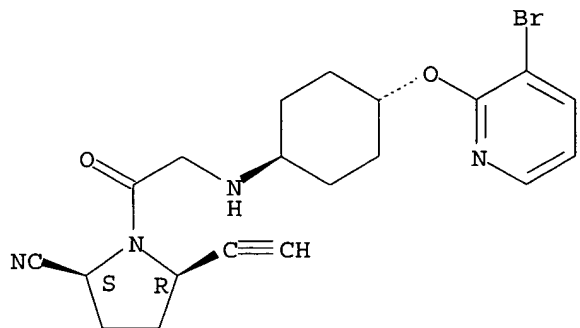
Absolute stereochemistry.



RN 676561-50-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(3-bromo-2-pyridinyl)oxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)-(9CI) (CA INDEX NAME)

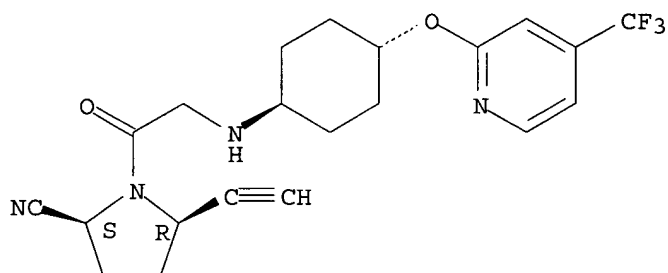
Absolute stereochemistry.



RN 676561-51-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[4-(trifluoromethyl)-2-pyridinyl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

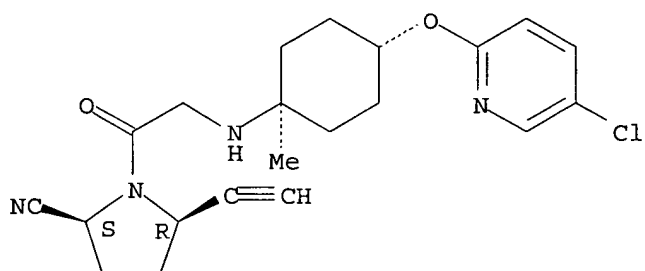
Absolute stereochemistry.



RN 676561-52-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[[5-chloro-2-pyridinyl]oxy]-1-methylcyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

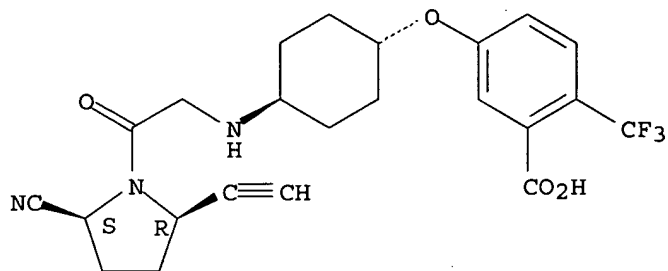
Absolute stereochemistry.



RN 676561-53-8 CAPLUS

CN Benzoic acid, 5-[[[trans-4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]cyclohexyl]oxy]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

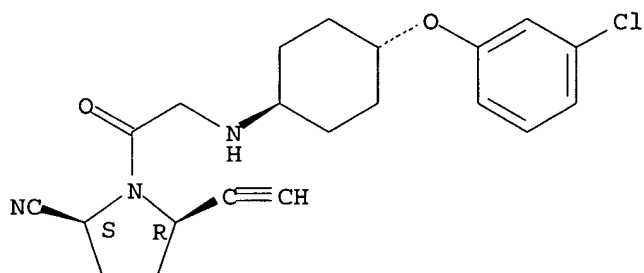
Absolute stereochemistry.



RN 676561-54-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(3-chlorophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

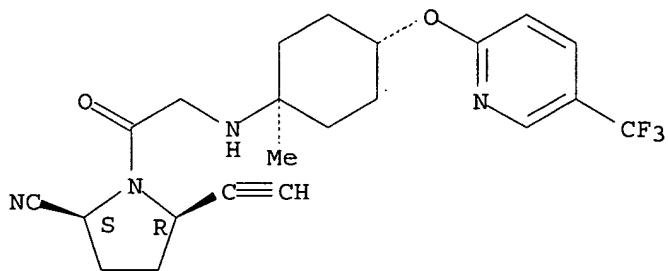
Absolute stereochemistry.



RN 676561-55-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-1-methyl-4-[[5-(trifluoromethyl)-2-pyridinyl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

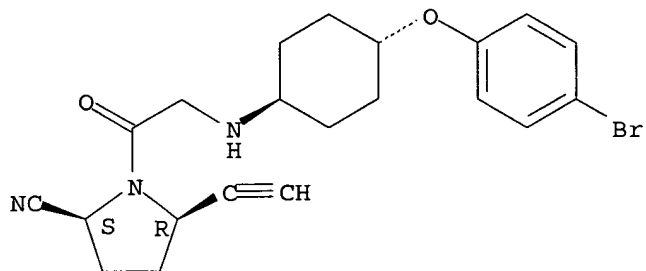
Absolute stereochemistry.



RN 676561-56-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(4-bromophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

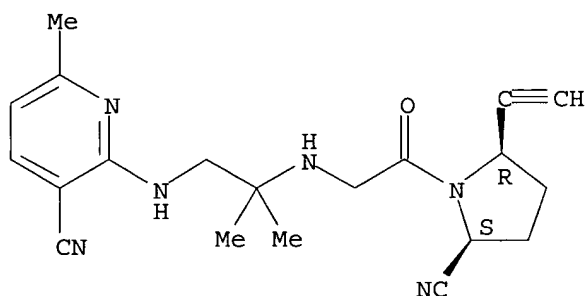
Absolute stereochemistry.



RN 676561-57-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(3-cyano-6-methyl-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

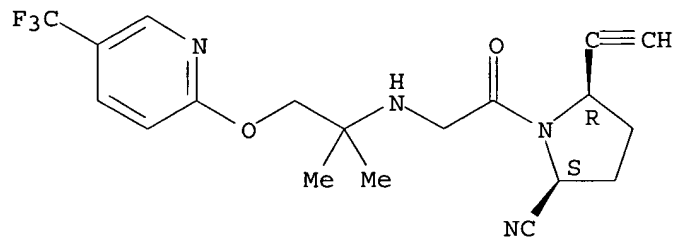
Absolute stereochemistry.



RN 676561-58-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1,1-dimethyl-2-[[5-(trifluoromethyl)-2-pyridinyl]oxy]ethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

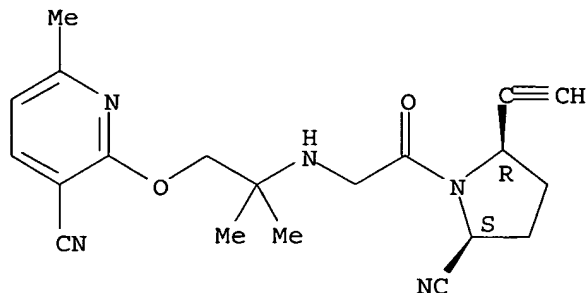
Absolute stereochemistry.



RN 676561-59-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(3-cyano-6-methyl-2-pyridinyl)oxy]-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

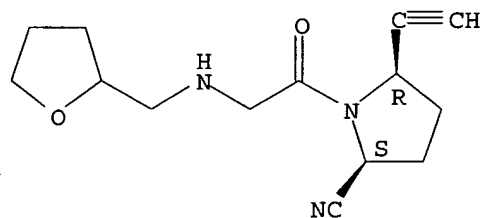
Absolute stereochemistry.



RN 676561-60-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[2-(4-cyanophenyl)ethoxy]methyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

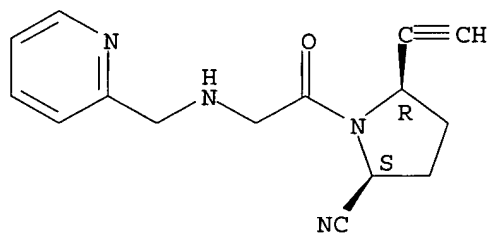
Absolute stereochemistry.



RN 676561-61-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[2-(pyridin-2-yl)methyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

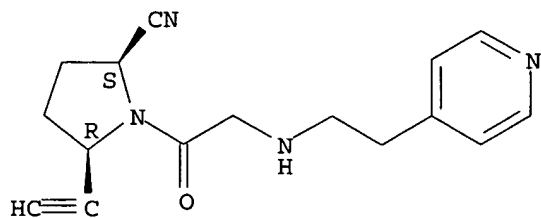
Absolute stereochemistry.



RN 676561-62-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[2-(4-pyridinyl)ethyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

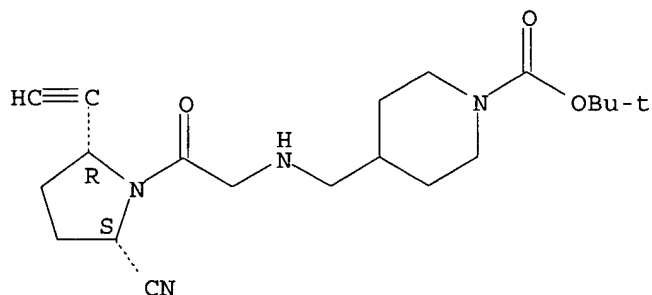
Absolute stereochemistry..



RN 676561-63-0 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]methyl]-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)

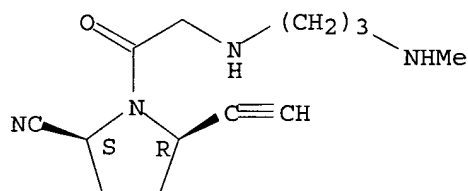
Absolute stereochemistry.



RN 676561-64-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[3-(methylamino)propyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

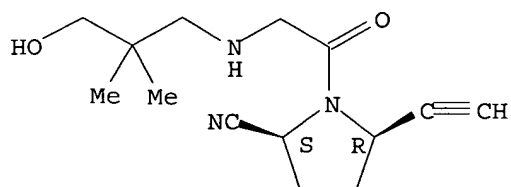
Absolute stereochemistry.



RN 676561-66-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[3-hydroxy-2,2-dimethylpropyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

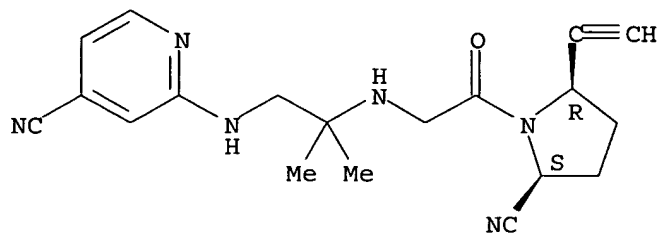
Absolute stereochemistry.



RN 676561-67-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(4-cyano-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

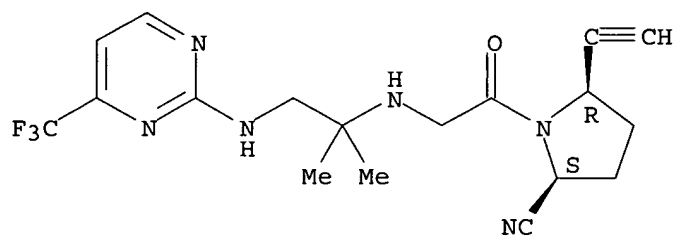
Absolute stereochemistry.



RN 676561-68-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1,1-dimethyl-2-[[4-(trifluoromethyl)-2-pyrimidinyl]amino]ethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

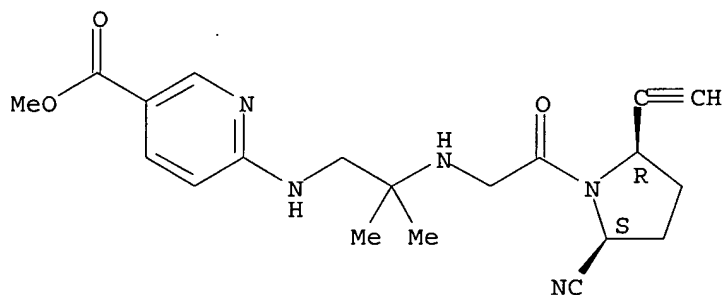
Absolute stereochemistry.



RN 676561-69-6 CAPLUS

CN 3-Pyridinecarboxylic acid, 6-[[2-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-2-methylpropyl]amino]-, methyl ester (9CI) (CA INDEX NAME)

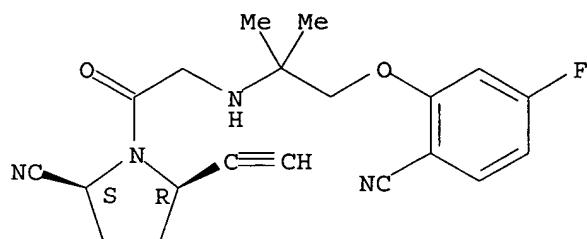
Absolute stereochemistry.



RN 676561-70-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-(2-cyano-5-fluorophenoxy)-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

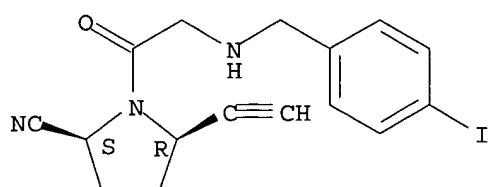
Absolute stereochemistry.



RN 676561-71-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(4-iodophenyl)methyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

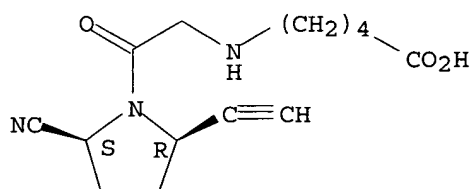
Absolute stereochemistry.



RN 676561-73-2 CAPLUS

CN Pentanoic acid, 5-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

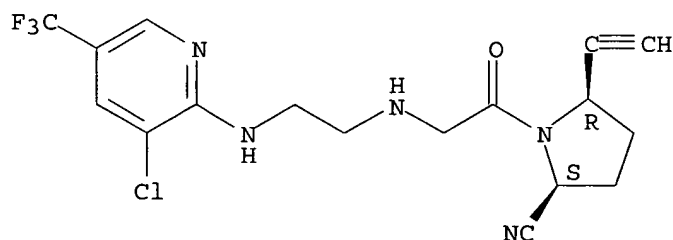
Absolute stereochemistry.



RN 676561-74-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]amino]ethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

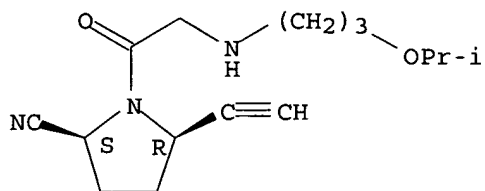
Absolute stereochemistry.



RN 676561-75-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[3-(1-methylethoxy)propyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

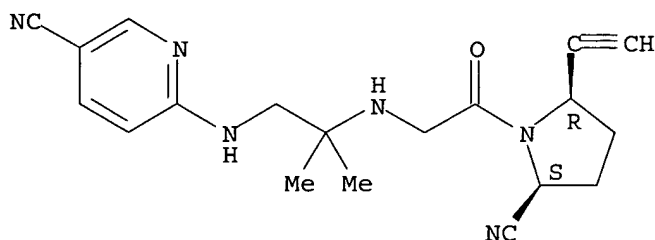
Absolute stereochemistry.



RN 676561-76-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(5-cyano-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

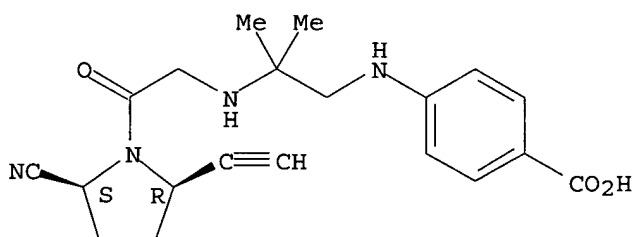
Absolute stereochemistry.



RN 676561-78-7 CAPLUS

CN Benzoic acid, 4-[[2-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-2-methylpropyl]amino]-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

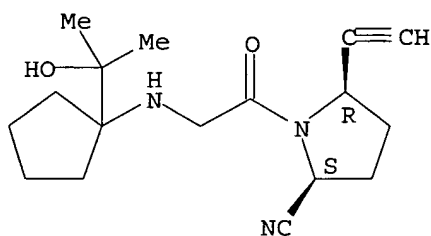


●x HCl

RN 676561-79-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1-(1-hydroxy-1-methylethyl)cyclopentyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

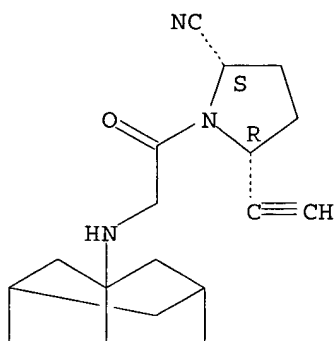
Absolute stereochemistry.



RN 676561-81-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[hexahydro-2,5-methanopentalen-3a(1H)-yl]amino]acetyl-, (2S,5R)- (9CI) (CA INDEX NAME)

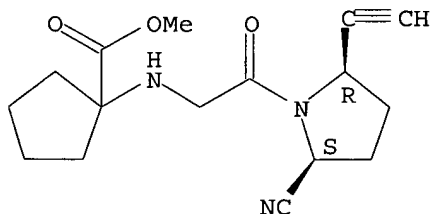
Absolute stereochemistry.



RN 676561-82-3 CAPLUS

CN Cyclopentanecarboxylic acid, 1-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-, methyl ester (9CI) (CA INDEX NAME)

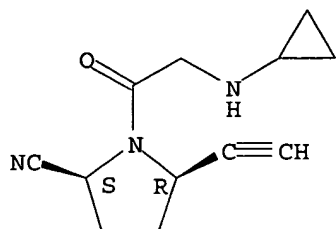
Absolute stereochemistry.



RN 676561-83-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclopropylamino)acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

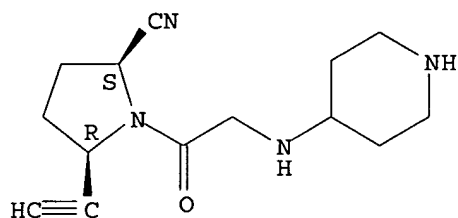
Absolute stereochemistry.



RN 676561-84-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[(4-piperidinylamino)acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

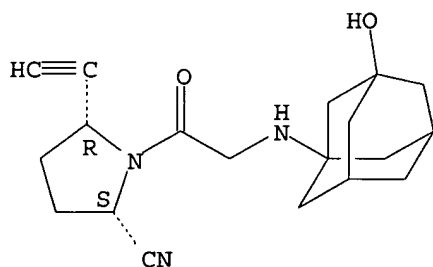
Absolute stereochemistry.



RN 676561-85-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[3-hydroxytricyclo[3.3.1.1.3,7]dec-1-yl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

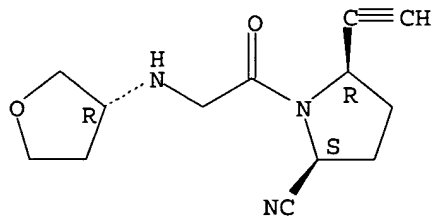
Absolute stereochemistry.



RN 676561-86-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[3-hydroxytricyclo[3.3.1.1.3,7]dec-1-yl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

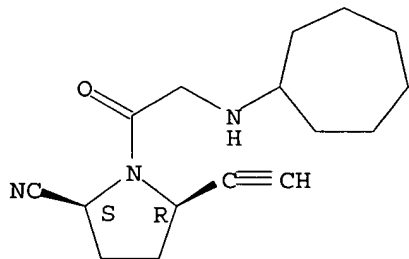
Absolute stereochemistry.



RN 676561-87-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cycloheptylamino)acetyl]-5-ethynyl-,
(2S,5R)- (9CI) (CA INDEX NAME)

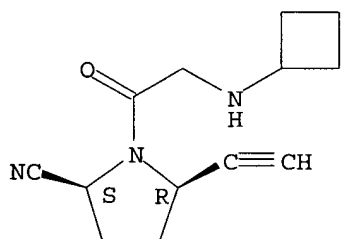
Absolute stereochemistry.



RN 676561-88-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclobutylamino)acetyl]-5-ethynyl-,
(2S,5R)- (9CI) (CA INDEX NAME)

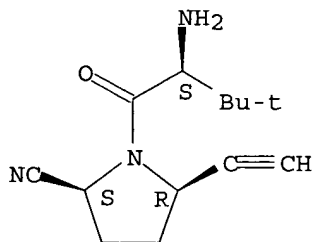
Absolute stereochemistry.



RN 676561-89-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

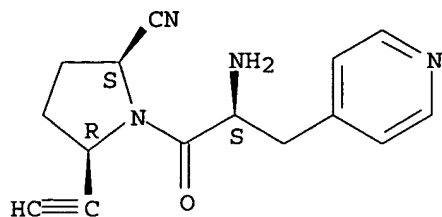
Absolute stereochemistry.



RN 676561-90-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-1-oxo-3-(4-pyridinyl)propyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

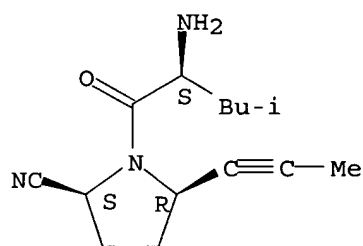
Absolute stereochemistry.



RN 676561-92-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

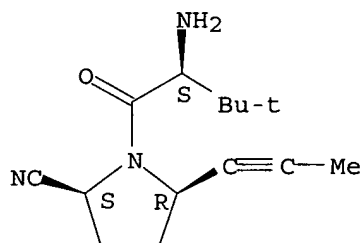
Absolute stereochemistry.



RN 676561-93-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

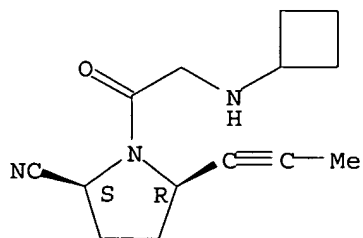
Absolute stereochemistry.



RN 676561-94-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclobutylamino)acetyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

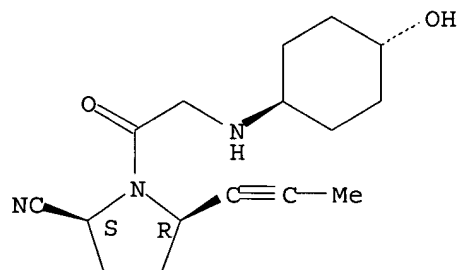
Absolute stereochemistry.



RN 676561-95-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(trans-4-hydroxycyclohexyl)amino]acetyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

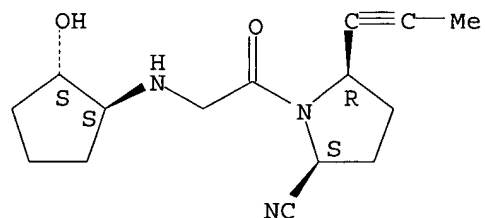
Absolute stereochemistry.



RN 676561-96-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(1S,2S)-2-hydroxycyclopentyl]amino]acetyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

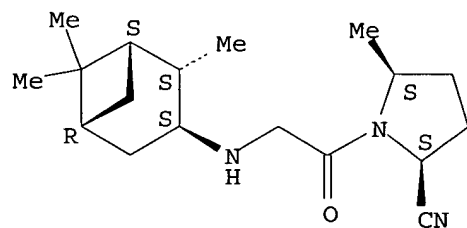
Absolute stereochemistry.



RN 676561-97-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-methyl-1-[[[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino]acetyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

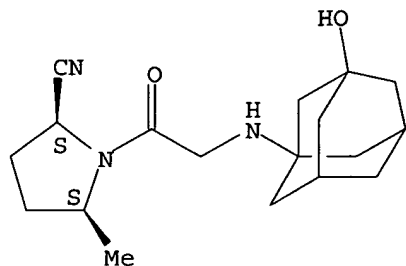
Absolute stereochemistry.



RN 676561-98-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-hydroxytricyclo[3.3.1.1^{3,7}]dec-1-yl)amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

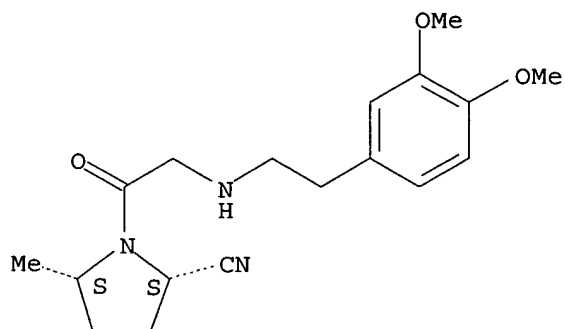
Absolute stereochemistry.



RN 676561-99-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-(3,4-dimethoxyphenyl)ethyl]amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

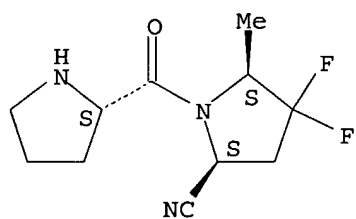
Absolute stereochemistry.



RN 676562-00-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-5-methyl-1-[(2S)-2-pyrrolidinylcarbonyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

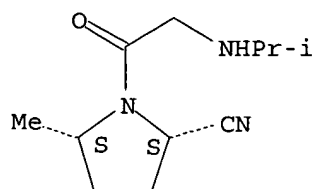
Absolute stereochemistry.



RN 676562-02-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-methyl-1-[[[(1-methylethyl)amino]acetyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

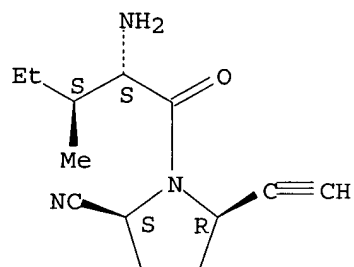
Absolute stereochemistry.



RN 676562-03-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

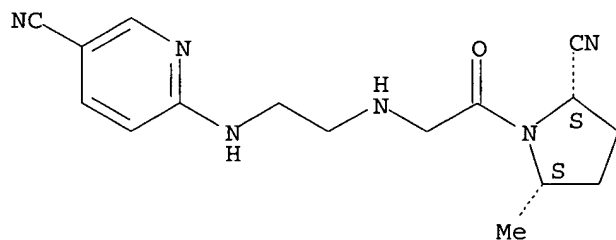
Absolute stereochemistry.



RN 676562-04-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(5-cyano-2-pyridinyl)amino]ethyl]amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

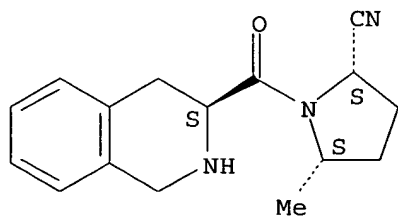
Absolute stereochemistry.



RN 676562-05-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-methyl-1-[[[(3S)-1,2,3,4-tetrahydro-3-isoquinoliny]carbonyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

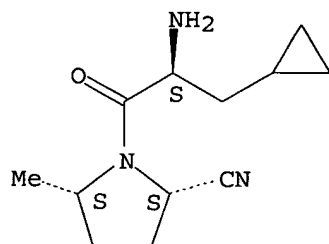
Absolute stereochemistry.



RN 676562-06-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3-cyclopropyl-1-oxopropyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

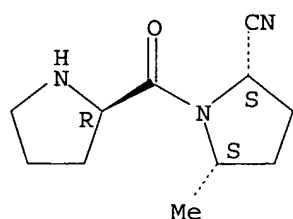
Absolute stereochemistry.



RN 676562-07-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-methyl-1-[(2R)-2-pyrrolidinylcarbonyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

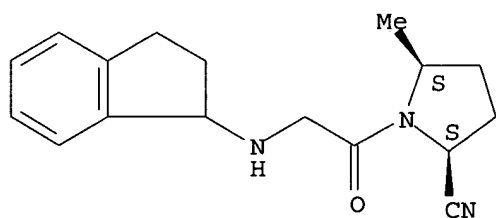
Absolute stereochemistry.



RN 676562-08-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(2,3-dihydro-1H-inden-1-yl)amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

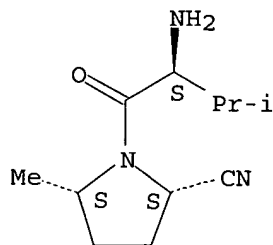
Absolute stereochemistry.



RN 676562-09-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3-methyl-1-oxobutyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

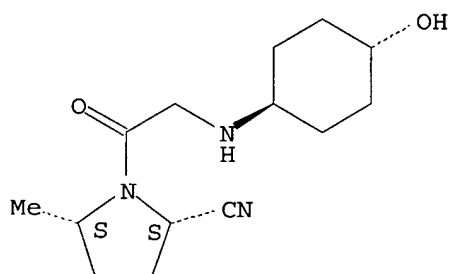
Absolute stereochemistry.



RN 676562-10-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(trans-4-hydroxycyclohexyl) amino] acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

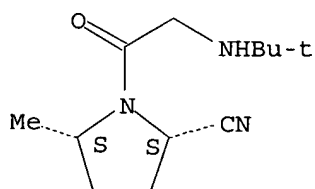
Absolute stereochemistry.



RN 676562-11-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(1,1-dimethylethyl) amino] acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

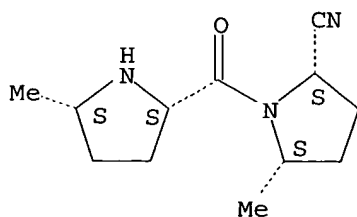
Absolute stereochemistry.



RN 676562-12-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-methyl-1-[[[(2S,5S)-5-methyl-2-pyrrolidinyl] carbonyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

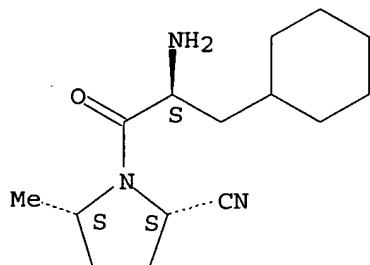
Absolute stereochemistry.



RN 676562-13-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3-cyclohexyl-1-oxopropyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

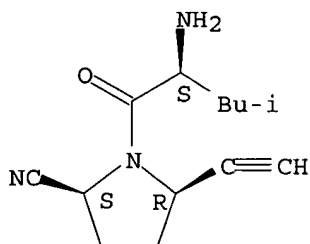
Absolute stereochemistry.



RN 676562-14-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

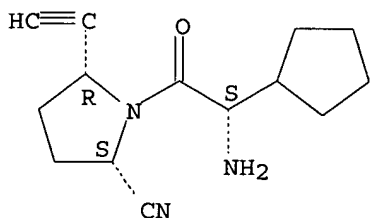
Absolute stereochemistry.



RN 676562-15-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclopentylacetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

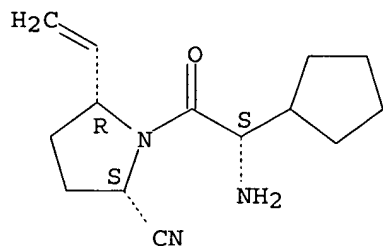
Absolute stereochemistry.



RN 676562-16-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclopentylacetyl]-5-ethenyl-, (2S,5R)- (9CI) (CA INDEX NAME)

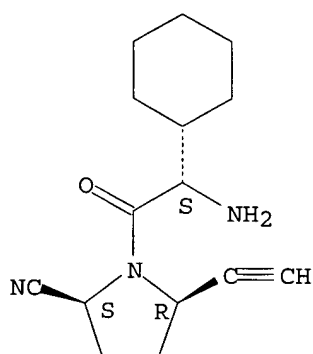
Absolute stereochemistry.



RN 676562-18-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclohexylacetyl]-5-ethynyl-,
(2S,5R)- (9CI) (CA INDEX NAME)

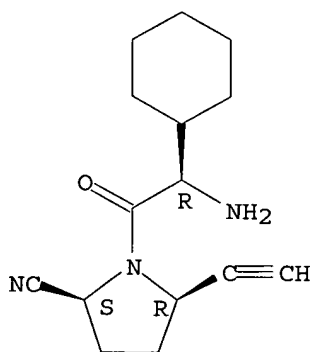
Absolute stereochemistry.



RN 676562-19-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2R)-aminocyclohexylacetyl]-5-ethynyl-,
(2S,5R)- (9CI) (CA INDEX NAME)

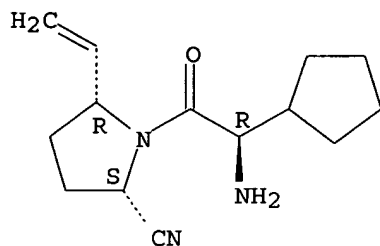
Absolute stereochemistry.



RN 676562-20-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2R)-aminocyclopentylacetyl]-5-ethynyl-,
(2S,5R)- (9CI) (CA INDEX NAME)

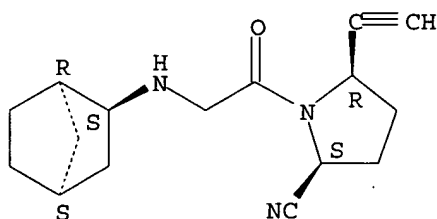
Absolute stereochemistry.



RN 676562-21-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(1R,2S,4S)-bicyclo[2.2.1]hept-2-ylamino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

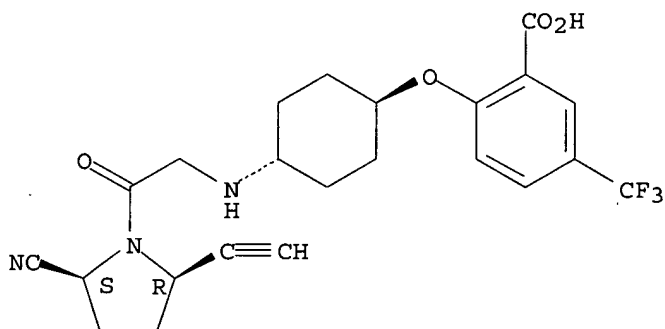
Absolute stereochemistry.



RN 676562-22-4 CAPLUS

CN Benzoic acid, 2-[[[trans-4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]cyclohexyl]oxy]-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)

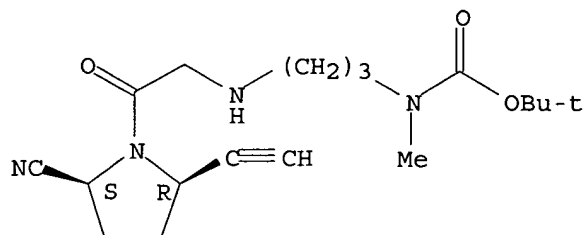
Absolute stereochemistry.



RN 676562-23-5 CAPLUS

CN Carbamic acid, [3-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]propyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

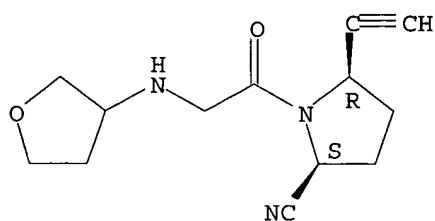
Absolute stereochemistry.



RN 676562-24-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[tetrahydro-3-furanyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

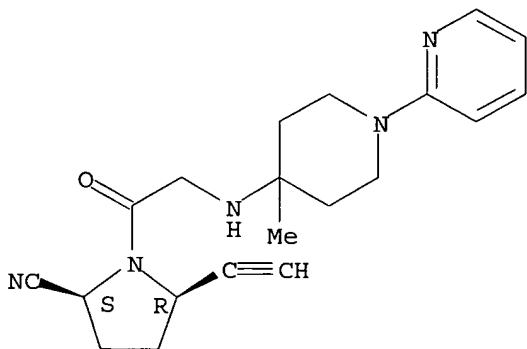
Absolute stereochemistry.



RN 676562-25-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-(2-pyridinyl)-4-piperidinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

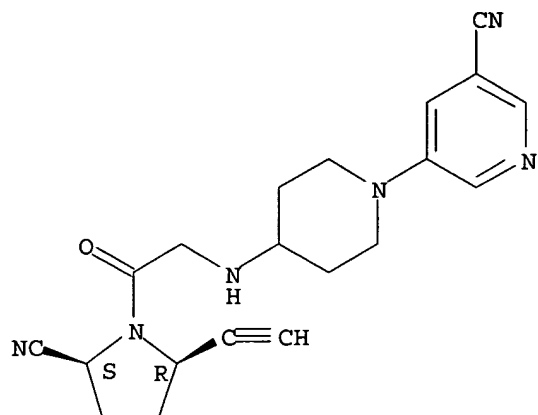
Absolute stereochemistry.



RN 676562-26-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-3-pyridinyl)-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

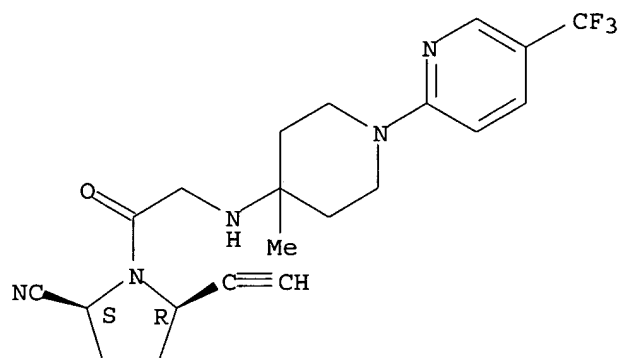
Absolute stereochemistry.



RN 676562-27-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[5-(trifluoromethyl)-2-pyridinyl]-4-piperidinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

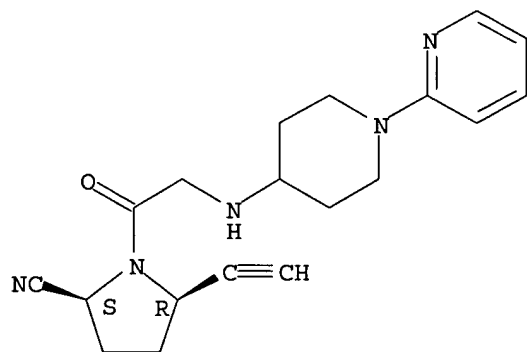
Absolute stereochemistry.



RN 676562-28-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1-(2-pyridinyl)-4-piperidinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

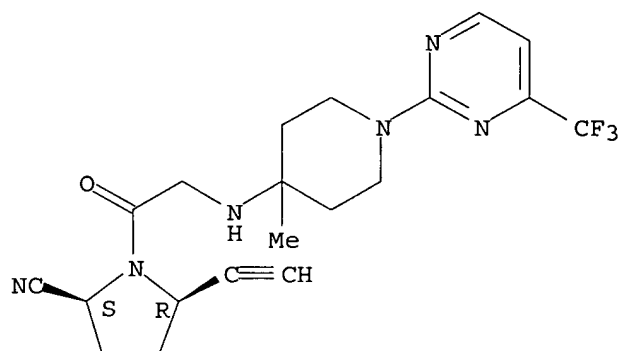
Absolute stereochemistry.



RN 676562-29-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[4-(trifluoromethyl)-2-pyrimidinyl]-4-piperidinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

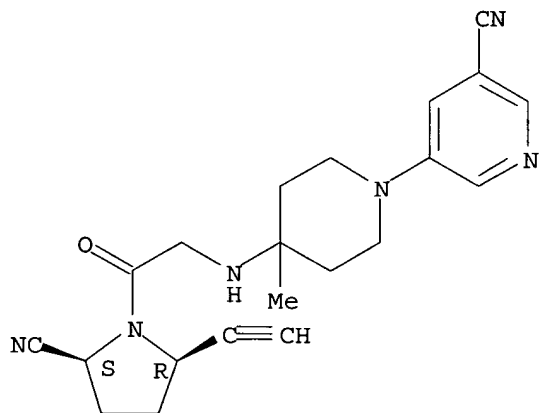
Absolute stereochemistry.



RN 676562-30-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-3-pyridinyl)-4-methyl-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

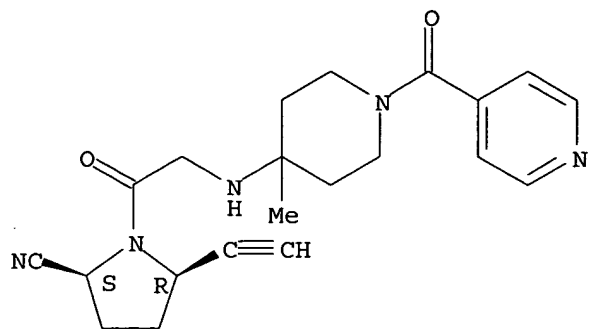
Absolute stereochemistry.



RN 676562-31-5 CAPLUS

CN 4-Piperidinamine, N-[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]-4-methyl-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

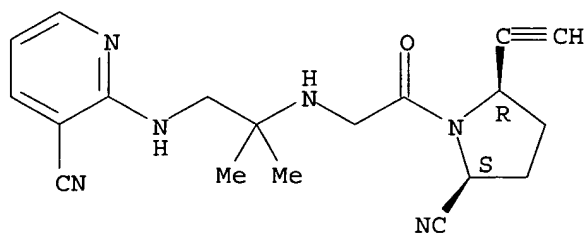
Absolute stereochemistry.



RN 676562-32-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(3-cyano-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

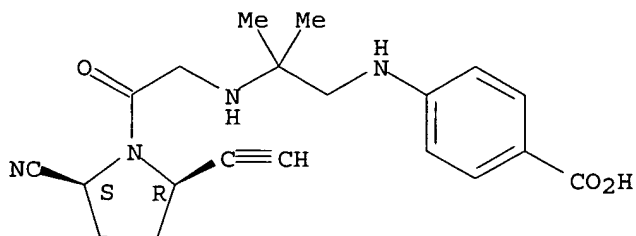
Absolute stereochemistry.



RN 676562-33-7 CAPLUS

CN Benzoic acid, 4-[[[2-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-2-methylpropyl]amino]- (9CI) (CA INDEX NAME)

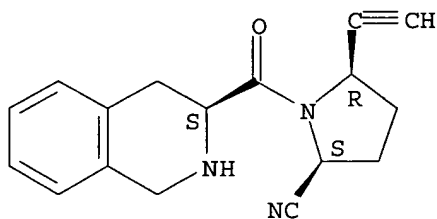
Absolute stereochemistry.



RN 676562-34-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(3S)-1,2,3,4-tetrahydro-3-isoquinoliny]carbonyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

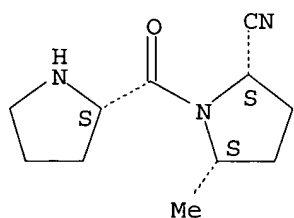
Absolute stereochemistry.



RN 676562-35-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-methyl-1-[(2S)-2-pyrrolidinylcarbonyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

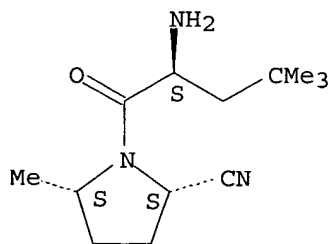
Absolute stereochemistry.



RN 676565-48-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4,4-dimethyl-1-oxopentyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

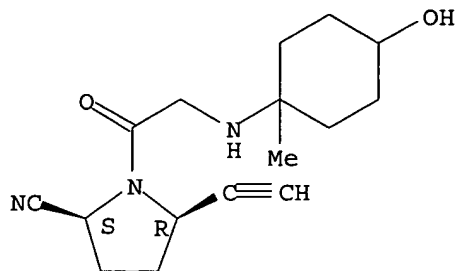
Absolute stereochemistry.



RN 676597-84-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[(4-hydroxy-1-methylcyclohexyl)amino]acetyl]-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

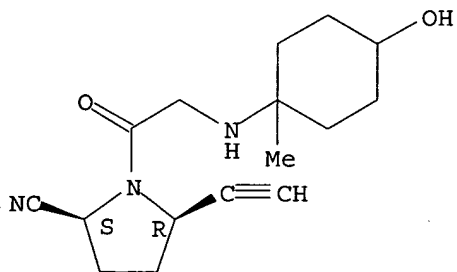


● HCl

RN 676597-85-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[4-(4-hydroxy-1-methylcyclohexyl)amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

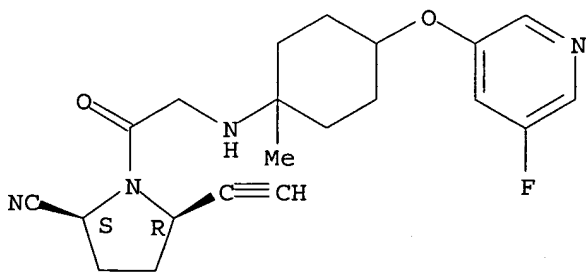
Absolute stereochemistry.



RN 676597-86-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[4-[(5-fluoro-3-pyridinyl)oxy]-1-methylcyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

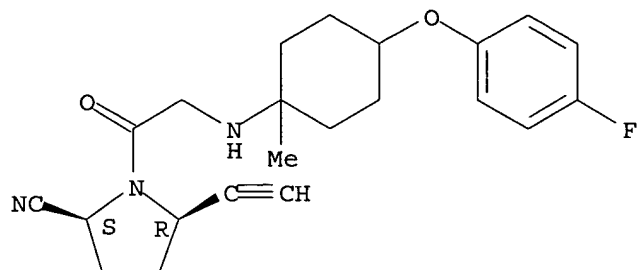
Absolute stereochemistry.



RN 676597-87-8 CAPLUS

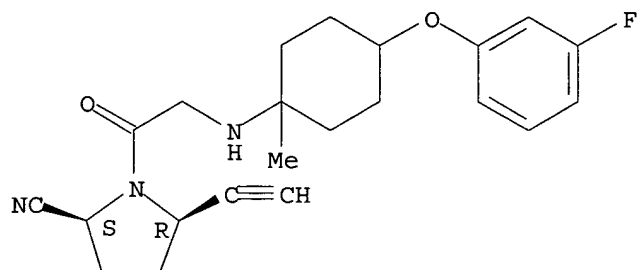
CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[4-(4-fluorophenoxy)-1-methylcyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



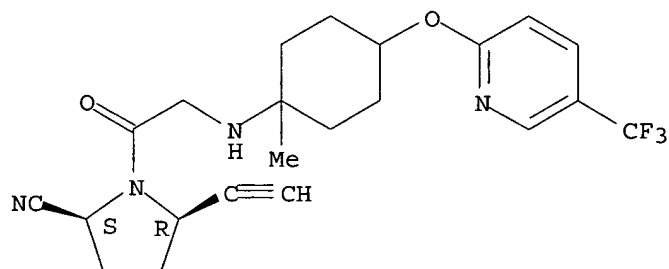
RN 676597-88-9 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-(3-fluorophenoxy)-1-methylcyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676597-89-0 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1-methyl-4-[[5-(trifluoromethyl)-2-pyridinyl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

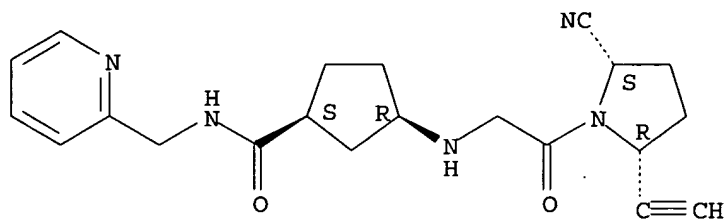
Absolute stereochemistry.



IT 813433-87-3P 813433-88-4P 813433-89-5P
 813433-90-8P 813433-91-9P 813433-92-0P
 813434-08-1P 813434-10-5P 815578-56-4P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of N-aminoacyl pyrrolidine-2-carbonitriles and related compds. as inhibitors of dipeptidyl peptidase-IV useful against type II diabetes and other disorders)
 RN 813433-87-3 CAPLUS
 CN Cyclopentanecarboxamide, 3-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-1-[[[4-(3-fluorophenoxy)-1-methylcyclohexyl]amino]acetyl]-, (2S,5R)- (9CI)

2-oxoethyl]amino]-N-(2-pyridinylmethyl)-, (1S,3R)- (9CI) (CA INDEX NAME)

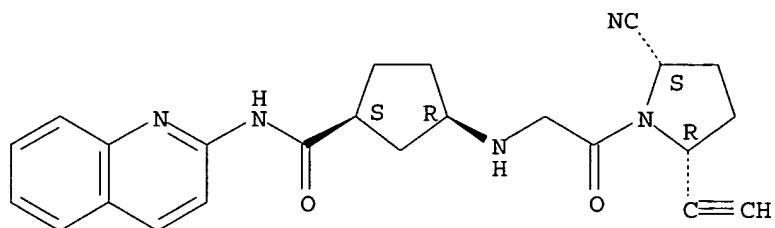
Absolute stereochemistry.



RN 813433-88-4 CAPLUS

CN Cyclopentanecarboxamide, 3-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-N-2-quinolinyl-, (1S,3R)- (9CI) (CA INDEX NAME)

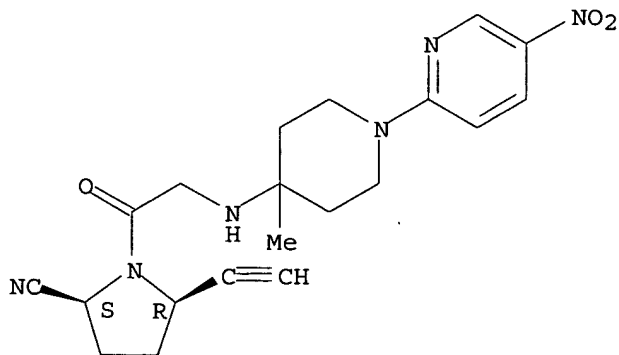
Absolute stereochemistry.



RN 813433-89-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-(5-nitro-2-pyridinyl)-4-piperidinyl]amino]acetyl]-, hydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



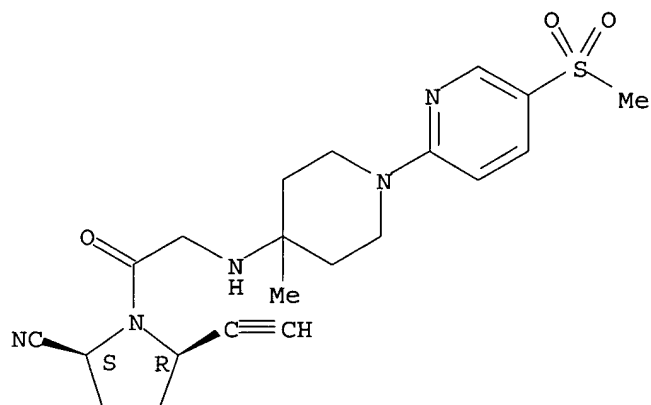
● x HCl

RN 813433-90-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[5-(methylsulfonyl)-2-pyridinyl]-4-piperidinyl]amino]acetyl]-, hydrochloride, (2S,5R)- (9CI)

(CA INDEX NAME)

Absolute stereochemistry.

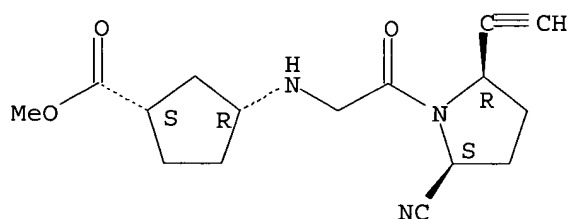


●x HCl

RN 813433-91-9 CAPLUS

CN Cyclopentanecarboxylic acid, 3-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-, methyl ester, (1S,3R)- (9CI) (CA INDEX NAME)

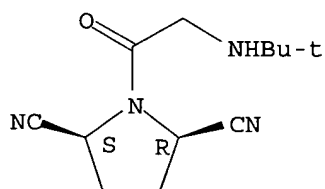
Absolute stereochemistry.



RN 813433-92-0 CAPLUS

CN 2,5-Pyrrolidinedicarbonitrile, 1-[[[(1,1-dimethylethyl)amino]acetyl]-, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

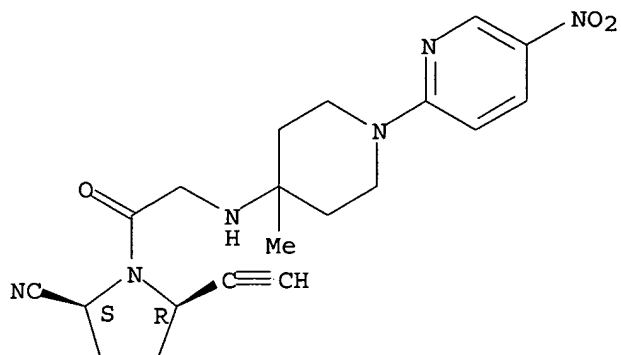


RN 813434-08-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-(5-nitro-2-pyridinyl)-

4-piperidinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

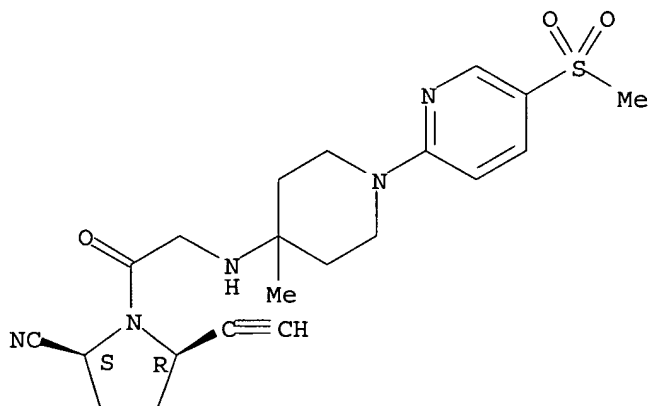
Absolute stereochemistry.



RN 813434-10-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[5-(methanesulfonyl)-2-pyridinyl]-4-piperidinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

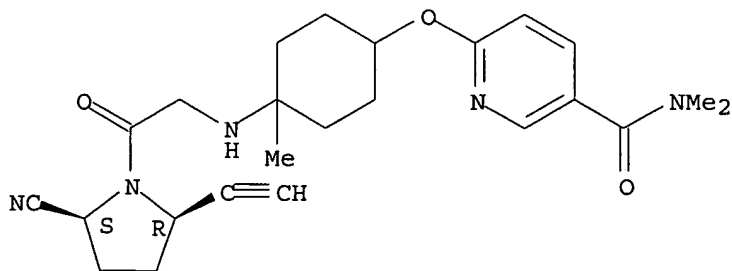
Absolute stereochemistry.



RN 815578-56-4 CAPLUS

CN 3-Pyridinecarboxamide, 6-[[[4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-4-methylcyclohexyl]oxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 676559-45-8P 676559-46-9P 676559-52-7P
 676559-53-8P 676559-55-0P 676559-60-7P
 676559-62-9P 676560-88-6P 676560-89-7P
 676560-95-5P 676560-96-6P 676561-18-5P
 676561-19-6P 676561-23-2P 676561-24-3P
 676561-25-4P 676561-77-6P

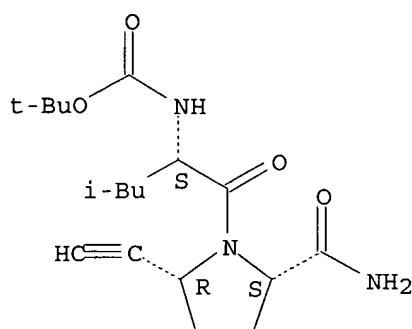
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of N-aminoacyl pyrrolidine-2-carbonitriles and related compds. as inhibitors of dipeptidyl peptidase-IV useful against type II diabetes and other disorders)

RN 676559-45-8 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl-5-ethynyl-, (5R)-(9CI) (CA INDEX NAME)

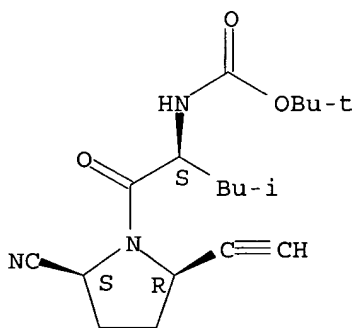
Absolute stereochemistry.



RN 676559-46-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

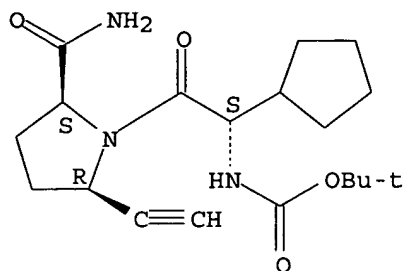
Absolute stereochemistry.



RN 676559-52-7 CAPLUS

CN L-Prolinamide, (2S)-2-cyclopentyl-N-[(1,1-dimethylethoxy)carbonyl]glycyl-5-ethynyl-, (5R)-(9CI) (CA INDEX NAME)

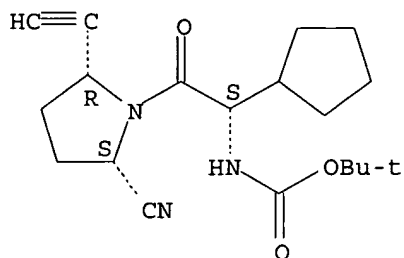
Absolute stereochemistry.



RN 676559-53-8 CAPLUS

CN Carbamic acid, [(1S)-2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-1-cyclopentyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

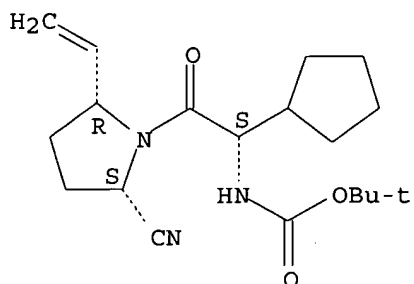
Absolute stereochemistry.



RN 676559-55-0 CAPLUS

CN Carbamic acid, [(1S)-2-[(2S,5R)-2-cyano-5-ethenyl-1-pyrrolidinyl]-1-cyclopentyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

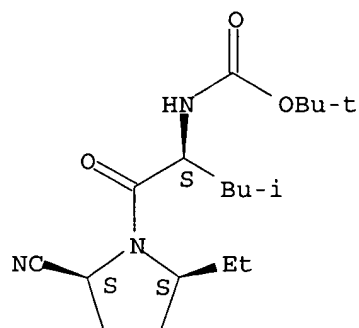
Absolute stereochemistry.



RN 676559-60-7 CAPLUS

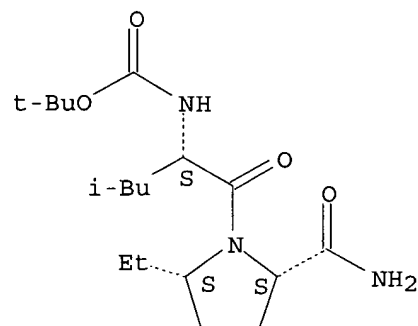
CN Carbamic acid, [(1S)-1-[[[(2S,5S)-2-cyano-5-ethyl-1-pyrrolidinyl]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



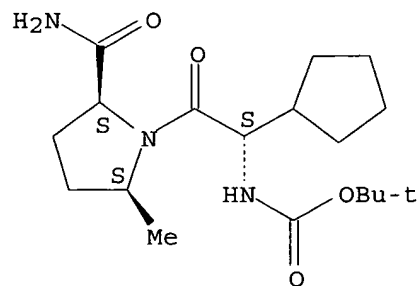
RN 676559-62-9 CAPLUS
 CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl-5-ethyl-, (5S)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



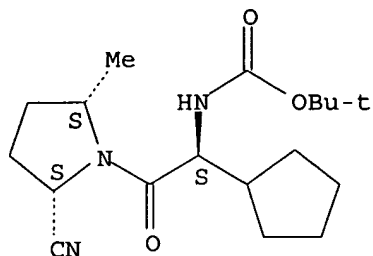
RN 676560-88-6 CAPLUS
 CN Carbamic acid, [(1S)-2-[(2S,5S)-2-(aminocarbonyl)-5-methyl-1-pyrrolidinyl]-1-cyclopentyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676560-89-7 CAPLUS
 CN Carbamic acid, [(1S)-2-[(2S,5S)-2-cyano-5-methyl-1-pyrrolidinyl]-1-cyclopentyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

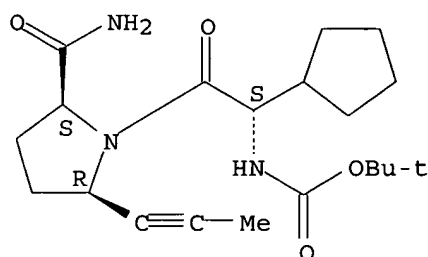
Absolute stereochemistry.



RN 676560-95-5 CAPLUS

CN L-Prolinamide, (2S)-2-cyclopentyl-N-[(1,1-dimethylethoxy)carbonyl]glycyl-5-(1-propynyl)-, (5R)- (9CI) (CA INDEX NAME)

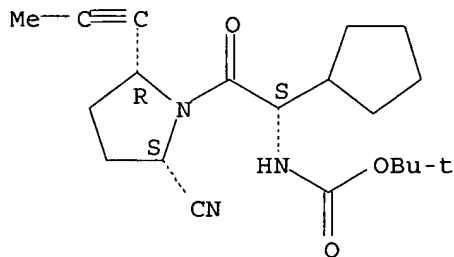
Absolute stereochemistry.



RN 676560-96-6 CAPLUS

CN Carbamic acid, [(1S)-2-[(2S,5R)-2-cyano-5-(1-propynyl)-1-pyrrolidinyl]-1-cyclopentyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

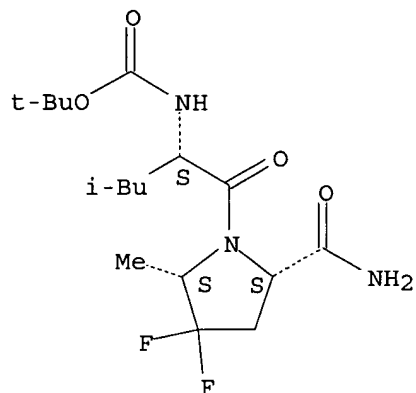
Absolute stereochemistry.



RN 676561-18-5 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl-4,4-difluoro-5-methyl-, (5S)- (9CI) (CA INDEX NAME)

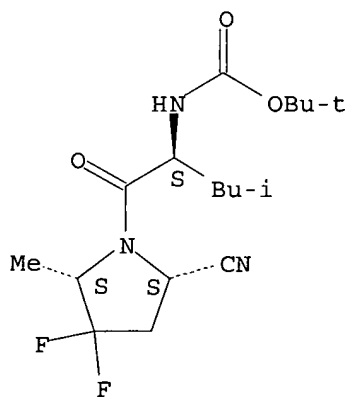
Absolute stereochemistry.



RN 676561-19-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(2S,5S)-5-cyano-3,3-difluoro-2-methyl-1-pyrrolidinyl]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

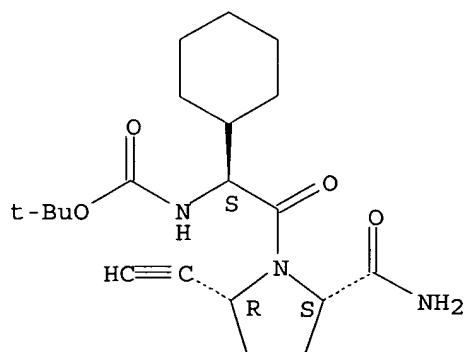
Absolute stereochemistry.



RN 676561-23-2 CAPLUS

CN L-Prolinamide, (2S)-2-cyclohexyl-N-[(1,1-dimethylethoxy)carbonyl]glycyl-5-ethynyl-, (5R)- (9CI) (CA INDEX NAME)

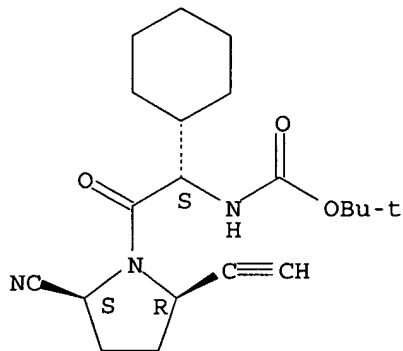
Absolute stereochemistry.



RN 676561-24-3 CAPLUS

CN Carbamic acid, [(1S)-2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-1-cyclohexyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

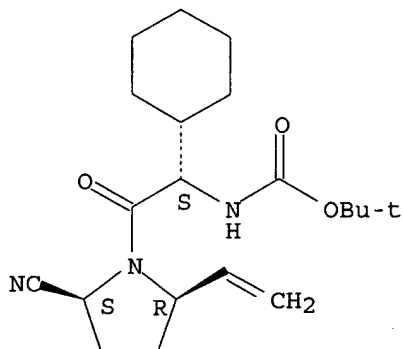
Absolute stereochemistry.



RN 676561-25-4 CAPLUS

CN Carbamic acid, [(1S)-2-[(2S,5R)-2-cyano-5-ethenyl-1-pyrrolidinyl]-1-cyclohexyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

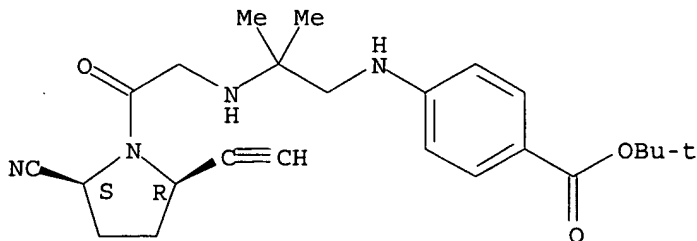
Absolute stereochemistry.



RN 676561-77-6 CAPLUS

CN Benzoic acid, 4-[[2-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-2-methylpropyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

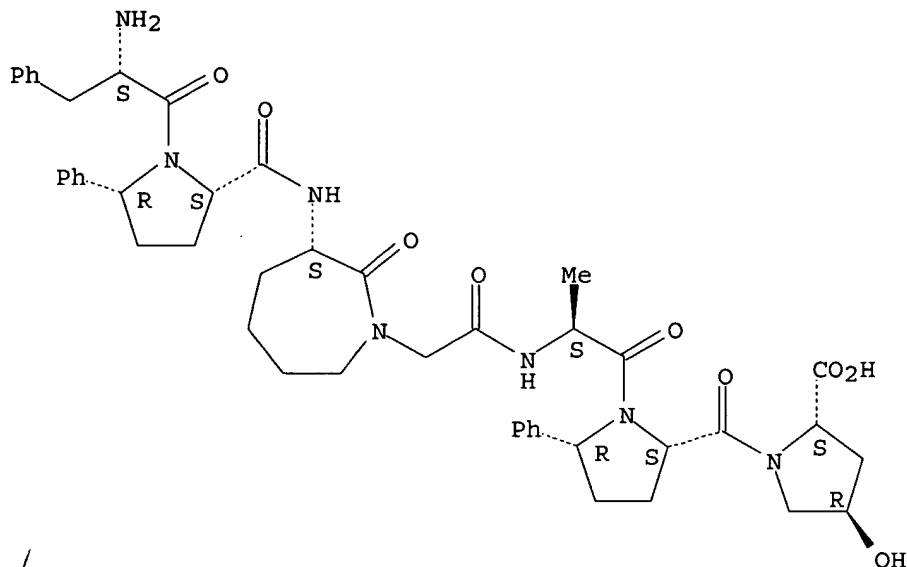
Absolute stereochemistry.



L51 ANSWER 7 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:610028 CAPLUS
 DOCUMENT NUMBER: 141:150947
 TITLE: Affinity fishing for ligands and protein receptors by
 an efficient process involving protein mixtures and
 ligand libraries
 INVENTOR(S): St. Hilaire, Phaedria Marie; Yin, Haifeng; Surve,
 Sheryl; Wenckens, Martin
 PATENT ASSIGNEE(S): Carlsberg A/S, Den.
 SOURCE: PCT Int. Appl., 172 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: **Patent**
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2004062553 | A2 | 20040729 | WO 2004-DK23 | 20040116 |
| WO 2004062553 | A3 | 20050127 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ | | | | |
| US 2004142379 | A1 | 20040722 | US 2003-346737 | 20030116 |
| AU 2004204276 | A1 | 20040729 | AU 2004-204276 | 20040116 |
| EP 1588173 | A2 | 20051026 | EP 2004-702645 | 20040116 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| PRIORITY APPLN. INFO.: | | | US 2003-346737 | A 20030116 |
| | | | DK 2003-749 | A 20030519 |
| | | | WO 2004-DK23 | W 20040116 |
| AB The invention provides putative "drugable" protein targets and actively binding ligands identified in an efficient and reproducible process by determining the affinity of protein mixts. to libraries of ligand compds. of defined size and composition The libraries are used to isolate and identify previously unknown corresponding protein-ligand binding pairs from a mixture of proteins and a library of compds., and are particularly useful to identify differentially selective protein-ligand binding pairs, for example, representing a single physiol. state or several varied but related states, such as disease vs. normal conditions. The invention also provides processes for identifying such protein-ligand binding pairs. | | | | |
| IT 724785-47-1P RL: BSU (Biological study, unclassified); CPN (Combinatorial preparation); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses) (affinity fishing for ligands and protein receptors by an efficient process involving protein mixts. and ligand libraries) | | | | |
| RN 724785-47-1 CAPLUS | | | | |
| CN L-Proline, L-phenylalanyl-(5R)-5-phenyl-L-prolyl-(3S)-3-aminohexahydro-2- oxo-1H-azepine-1-acetyl-L-alanyl-(5R)-5-phenyl-L-prolyl-4-hydroxy-, (4R)- (9CI) (CA INDEX NAME) | | | | |

Absolute stereochemistry.



✓ L51 ANSWER 8 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:589139 CAPLUS
 DOCUMENT NUMBER: 141:140767
 TITLE: Affinity fishing for ligands and protein receptors
 INVENTOR(S): St. Hilaire, Phaedria Marie; Yin, Haifeng; Surve, Sheryl
 PATENT ASSIGNEE(S): Carlsberg Research Laboratory, Den.
 SOURCE: U.S. Pat. Appl. Publ., 55 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| US 2004142379 | A1 | 20040722 | US 2003-346737 | 20030116 |
| AU 2004204276 | A1 | 20040729 | AU 2004-204276 | 20040116 |
| WO 2004062553 | A2 | 20040729 | WO 2004-DK23 | 20040116 |
| WO 2004062553 | A3 | 20050127 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ | | | | |
| EP 1588173 | A2 | 20051026 | EP 2004-702645 | 20040116 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| PRIORITY APPLN. INFO.: | | | US 2003-346737 | A 20030116 |
| | | | DK 2003-749 | A 20030519 |
| | | | WO 2004-DK23 | W 20040116 |

AB The invention provides a process for identifying specific members of a previously unknown protein-ligand binding pair which comprises the steps of (a) synthesizing a ligand library onto resin beads to form an immobilized ligand library, (b) incubating the immobilized ligand library with one or more protein mixts., (c) detecting an immobilized ligand-protein binding pair from the incubation mixture, and (d) identifying

the ligand and the protein of the ligand-binding pair. The identified ligand and protein are specific members of a previously unknown ligand-protein binding pair, which, e.g., represent a single physiological state or several varied but related states, such as disease vs. normal conditions. Thus, a peptide library which contains a photolabile linker and a spacer was used in solid-phase screening of labeled myocyte proteins.

IT 724785-47-1P

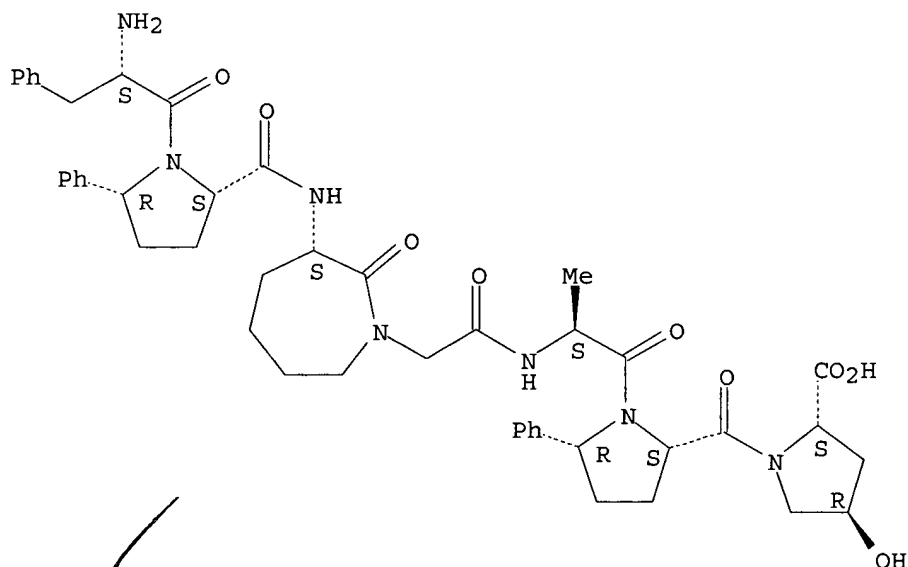
RL: ANT (Analyte); DGN (Diagnostic use); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(affinity fishing for ligands and proteins receptors)

RN 724785-47-1 CAPLUS

CN L-Proline, L-phenylalanyl-(5R)-5-phenyl-L-prolyl-(3S)-3-aminohexahydro-2-oxo-1H-azepine-1-acetyl-L-alanyl-(5R)-5-phenyl-L-prolyl-4-hydroxy-, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 9 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:331906 CAPLUS

DOCUMENT NUMBER: 140:339636

TITLE: Preparation of amino acid benzylamide derivatives as thrombin inhibitors

INVENTOR(S): Staas, Donnette D.; Lyle, Terry A.; Williams, Peter D.; Sanderson, Philip E. J.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 127 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

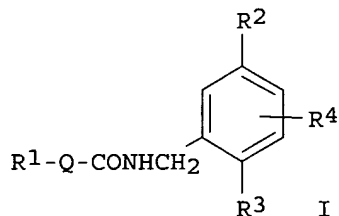
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|-------|-----------------|-------|
| ----- | ---- | ----- | ----- | ----- |

WO 2004032834 A2 20040422 WO 2003-US30867 20030930
 WO 2004032834 A3 20040610
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
 GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
 PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
 TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 AU 2003299901 A1 20040504 AU 2003-299901 20030930
 PRIORITY APPLN. INFO.: US 2002-415976P P 20021004
 WO 2003-US30867 W 20030930
 OTHER SOURCE(S): MARPAT 140:339636
 GI

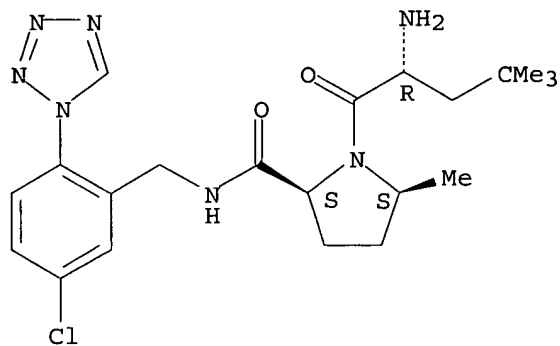


AB Compds. I [Q-CO is proline substituted by F, N3, NH2, OH or alkyl or 3,4-dehydropyrroline; R1 is acyl, including (un)substituted 2-azetidinecarbonyl, 2-pyrrolinecarbonyl, 2-piperidinecarbonyl, or 9-hydroxy-9-fluorene carbonyl; R2, R4 are H, halo, (cyclo)alkyl, CF3, OCF3, alkoxy or cyano; R3 is a 5-membered heteroaryl ring having 2-4 heteroatoms (at least 2 of which are N and at most 1 is S or O) or a 6-membered heteroaryl ring having 1-2 N atoms; the rings may be substituted by alkyl or halogen] or their pharmaceutically-acceptable salts were prepared as thrombin inhibitors. Thus, 4-methyl-D-leucyl-N-[5-chloro-2-(1H-tetrazol-1-yl)benzyl]-4,4-difluoroprolineamide (1) was prepared via peptide coupling reactions mediated by EDC and HOAT in DMF. Tablets containing 1 were prepared

IT 681128-03-0P 681128-15-4P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (Thrombin inhibitors)

RN 681128-03-0 CAPLUS
 CN L-Prolineamide, 4-methyl-D-leucyl-N-[[5-chloro-2-(1H-tetrazol-1-yl)phenyl]methyl]-5-methyl-, (5S)- (9CI) (CA INDEX NAME)

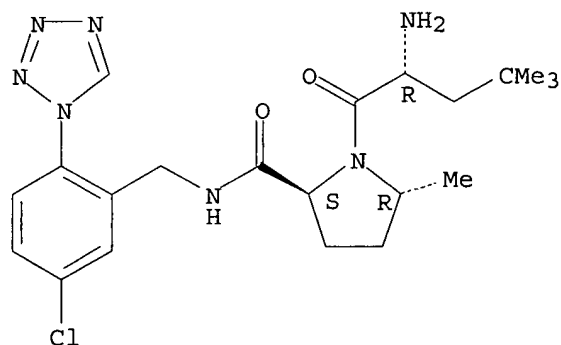
Absolute stereochemistry.



RN 681128-15-4 CAPLUS

CN L-Prolinamide, 4-methyl-D-leucyl-N-[[5-chloro-2-(1H-tetrazol-1-yl)phenyl]methyl]-5-methyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



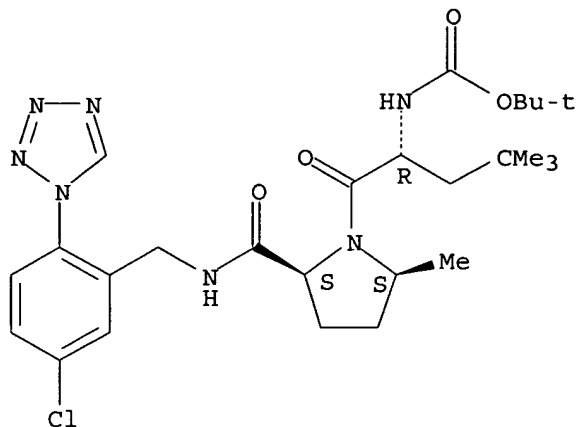
IT 681128-72-3P 681128-73-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(Thrombin inhibitors)

RN 681128-72-3 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-4-methyl-D-leucyl-N-[[5-chloro-2-(1H-tetrazol-1-yl)phenyl]methyl]-5-methyl-, (5S)- (9CI) (CA INDEX NAME)

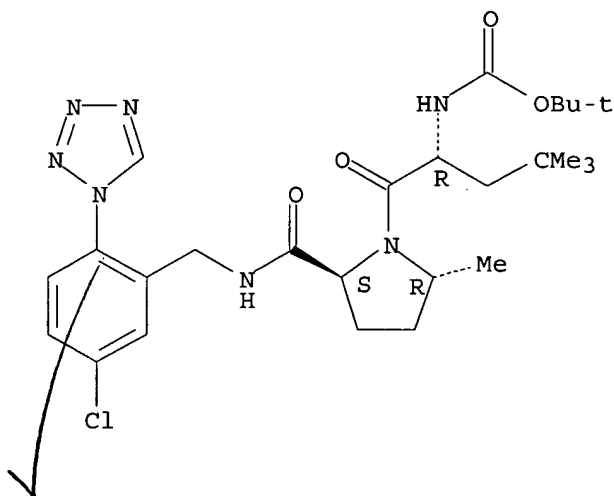
Absolute stereochemistry.



RN 681128-73-4 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-4-methyl-D-leucyl-N-[[5-chloro-2-(1H-tetrazol-1-yl)phenyl]methyl]-5-methyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 10 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:267291 CAPLUS

DOCUMENT NUMBER: 140:303518

TITLE: Preparation of N-aminoacyl pyrrolidine-2-carbonitriles and related compounds as inhibitors of dipeptidyl peptidase-IV (DPP-IV) useful against type II diabetes and other disorders

INVENTOR(S): Madar, David; Pei, Zhonghua; Pireh, Daisy; Djuric, Stevan W.; Wiedeman, Paul E.; Yong, Hong; Feenstra, Melissa J.; Kopecka, Hana; Li, Xiaofeng; Longenecker, Kenton; Sham, Hing L.; Stewart, Kent D.; Szczepankiewicz, Bruce G.

PATENT ASSIGNEE(S): Abbott Laboratories, USA

SOURCE: PCT Int. Appl., 135 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

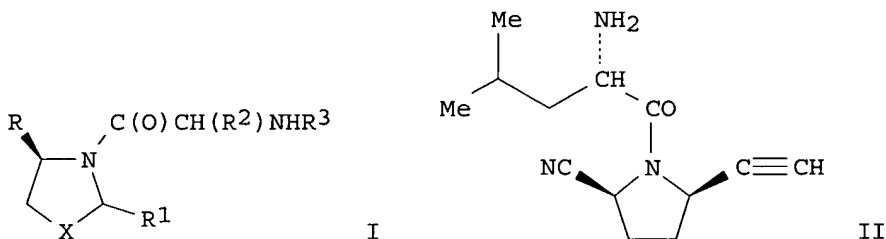
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------------------------|
| WO 2004026822 | A2 | 20040401 | WO 2003-US29018 | 20030915 |
| WO 2004026822 | A3 | 20040506 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004121964 | A1 | 20040624 | US 2003-659860 | 20030911 |
| CA 2497725 | AA | 20040401 | CA 2003-2497725 | 20030915 |
| AU 2003282800 | A1 | 20040408 | AU 2003-282800 | 20030915 |
| BR 2003014582 | A | 20050809 | BR 2003-14582 | 20030915 |
| EP 1560811 | A2 | 20050810 | EP 2003-774478 | 20030915 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2006503057 | T2 | 20060126 | JP 2004-537831 | 20030915 |
| ZA 2005002218 | A | 20050916 | ZA 2005-2218 | 20050316 |
| PRIORITY APPLN. INFO.: | | | | US 2002-246831 A 20020919 |
| | | | | US 2002-412084P P 20020919 |
| | | | | US 2003-659860 A 20030911 |
| | | | | WO 2003-US29018 W 20030915 |

OTHER SOURCE(S): MARPAT 140:303518

GI



AB The present invention relates to N-aminoacyl pyrrolidine-2-carbonitriles and related compds. (shown as I; variables defined below; e.g. II) that inhibit dipeptidyl peptidase IV (DPP-IV) and are useful for the prevention or treatment of **diabetes**, especially type II **diabetes**, as well as hyperglycemia, Syndrome X, hyperinsulinemia, obesity, atherosclerosis, and various immunomodulatory diseases (no data). Compds. I inhibit DPP-IV induced fluorescence with inhibitory consts. 0.014-7 μ M. Although the methods of preparation are not claimed, >100 example preps. are included. For example, II was prepared in 9 steps starting from Me (S)-(+)-2-pyrrolidone-5-carboxylate and involving intermediates di-Me (2S)-5-oxopyrrolidine-1,2-dicarboxylate, di-Me (2S)-5-methoxypyrrolidine-1,2-dicarboxylate, di-Me (2S)-5-[(trimethylsilyl)ethynyl]pyrrolidine-1,2-dicarboxylate (separated diastereomers), Me (5R)-5-[(trimethylsilyl)ethynyl]-L-

prolinate, Me (5R)-1-[N-(tert-butoxycarbonyl)-L-leucyl]-5-[(trimethylsilyl)ethynyl]-L-prolinate, (5R)-1-[N-(tert-butoxycarbonyl)-L-leucyl]-5-ethynyl-L-proline, (5R)-1-[N-(tert-butoxycarbonyl)-L-leucyl]-5-ethynyl-L-prolinamide and (5R)-1-[N-(tert-butoxycarbonyl)-L-leucyl]-5-ethynyl-L-pyrrolidine-2-carbonitrile. For I: X = CH₂, CHF and CF₂; R = alkylcarbonyl, arylcarbonyl, cyano, heterocyclecarbonyl, R₄R₅NC(O)-, B(OR₆)₂, 1,3,2-dioxaborolane and 4,4,5,5-tetramethyl-1,3,2-dioxaborolane; R₁ = alkoxyalkyl, alkyl, alkylcarbonyl, alkenyl, alkynyl, allenyl, arylalkyl, cycloalkyl, cycloalkylalkyl, cyano, haloalkyl, haloalkenyl, heterocyclealkyl, and hydroxyalkyl. R₂ and R₃ = H, alkoxyalkyl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocycle, heterocyclealkyl, hydroxyalkyl; or R₂ and R₃ taken together with the atoms to which they are attached form a mono or bicyclic heterocycle 2-indolinyl, 2-indolyl, 3-isoquinolinyl, 2-piperazinyl, 2-piperidinyl, 2-pyrrolidinyl, 2-pyrrolyl, 2-pyridinyl, 2-quinolinyl, 2-tetrahydroquinolinyl, and 3-tetrahydroisoquinolinyl, wherein said heterocycle may be substituted with 0-3 alkenyl, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylcarbonyl, alkylcarbonylalkyl, alkylcarbonyloxy, alkylsulfonyl, alkylthio, alkynyl, aryl, arylalkoxy, arylalkyl, arylcarbonyl, aryloxy, carboxy, carboxyalkyl, cyano, cyanoalkyl, formyl, halogen, haloalkyl, hydroxy, hydroxyalkyl, mercapto, nitro, Ph, R₄R₅N-, R₄R₅NC(O)-, and R₄R₅NCNS(O)₂-. R₄, R₅ and R₆ = H, alkyl, and arylalkyl; R_A and R_B = alkyl, alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl; or R_A and R_B taken together with the N to which they are attached form a ring piperidine, piperazine and morpholine; and R_C and R_D = H and alkyl.

IT 676560-63-7P 676561-27-6P 676561-65-2P
676561-72-1P

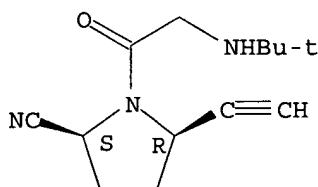
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(drug candidate; preparation of N-aminoacyl pyrrolidine-2-carbonitriles and related compds. as inhibitors of dipeptidyl peptidase-IV useful against type II **diabetes** and other disorders)

RN 676560-63-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(1,1-dimethylethyl)amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

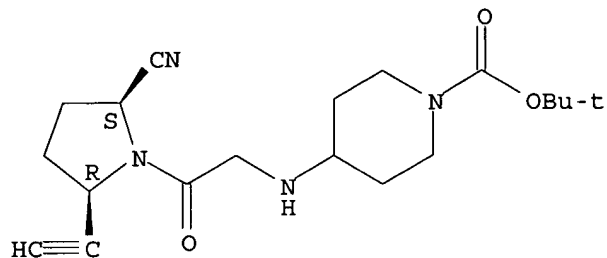
Absolute stereochemistry.



RN 676561-27-6 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

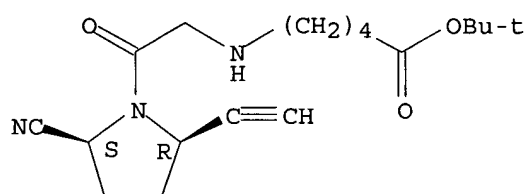
Absolute stereochemistry.



RN 676561-65-2 CAPLUS

CN Pentanoic acid, 5-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

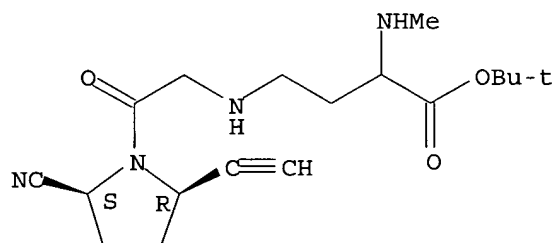
Absolute stereochemistry.



RN 676561-72-1 CAPLUS

CN Butanoic acid, 4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-2-(methylamino)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 676559-41-4P 676559-47-0P 676559-48-1P
 676559-54-9P 676559-56-1P 676559-57-2P
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676560-52-4P 676560-54-6P 676560-56-8P
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 676562-32-6P 676562-33-7P 676562-34-8P
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 676597-88-9P 676597-89-0P

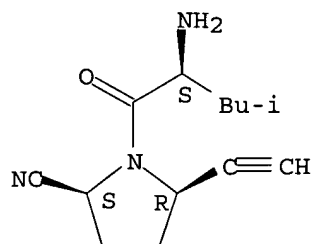
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(drug candidate; preparation of N-aminoacyl pyrrolidine-2-carbonitriles and
 related compds. as inhibitors of dipeptidyl peptidase-IV useful against
 type II **diabetes** and other disorders)

RN 676559-41-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-5-ethynyl-
 , monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

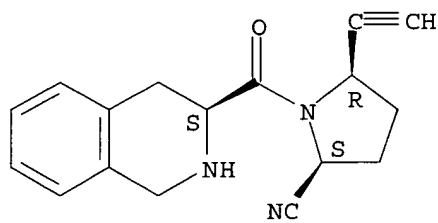
Absolute stereochemistry.



● HCl

RN 676559-47-0 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[1,2,3,4-tetrahydro-3-isoquinoliny]carbonyl]-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

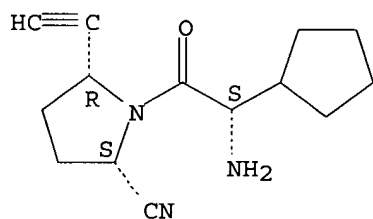
Absolute stereochemistry.



● HCl

RN 676559-48-1 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclopentylacetyl]-5-ethynyl-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

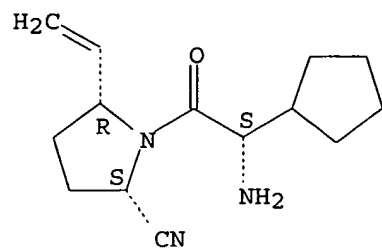
Absolute stereochemistry.



● HCl

RN 676559-54-9 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclopentylacetyl]-5-ethynyl-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

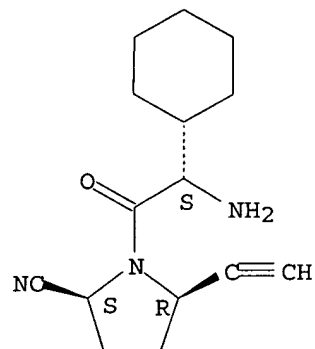


● HCl

RN 676559-56-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclohexylacetyl]-5-ethynyl-, monohydrochloride, (2S,5R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

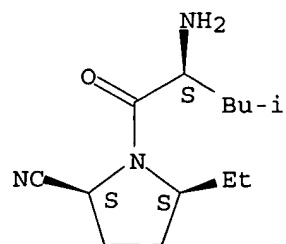


● HCl

RN 676559-57-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-5-ethyl-, (2S,5S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

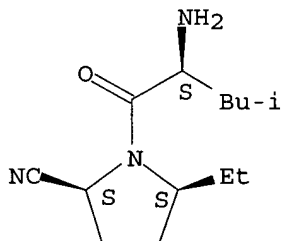


RN 676559-58-3 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-5-ethyl-,
 (2S,5S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

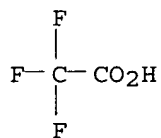
CRN 676559-57-2
 CMF C13 H23 N3 O

Absolute stereochemistry.



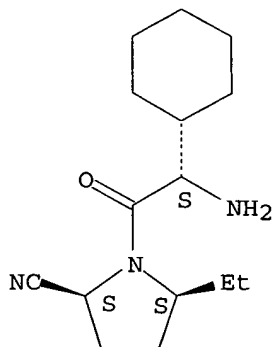
CM 2

CRN 76-05-1
 CMF C2 H F3 O2



RN 676559-63-0 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclohexylacetyl]-5-ethyl-,
 (2S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676559-64-1 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclohexylacetyl]-5-ethyl-,

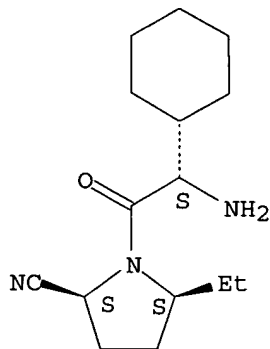
(2S,5S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 676559-63-0

CMF C15 H25 N3 O

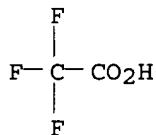
Absolute stereochemistry.



CM 2

CRN 76-05-1

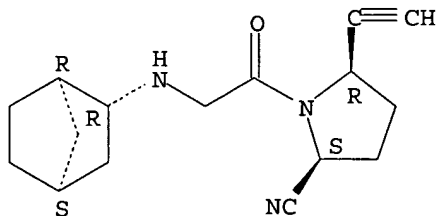
CMF C2 H F3 O2



RN 676559-65-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(1R,2R,4S)-bicyclo[2.2.1]hept-2-ylamino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

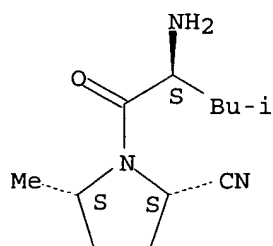
Absolute stereochemistry.



RN 676559-70-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

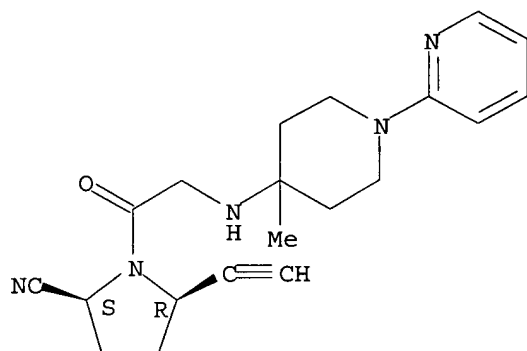
Absolute stereochemistry.



RN 676559-71-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-(2-pyridinyl)-4-piperidinyl]amino]acetyl]-, hydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

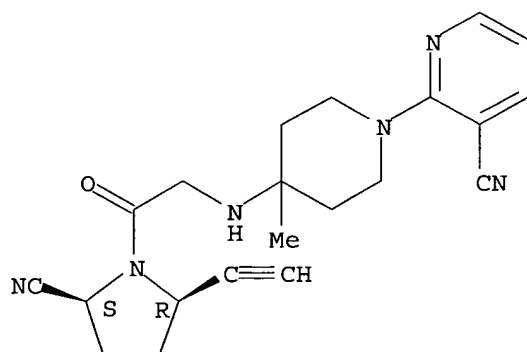


●x HCl

RN 676559-73-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(3-cyano-2-pyridinyl)-4-methyl-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

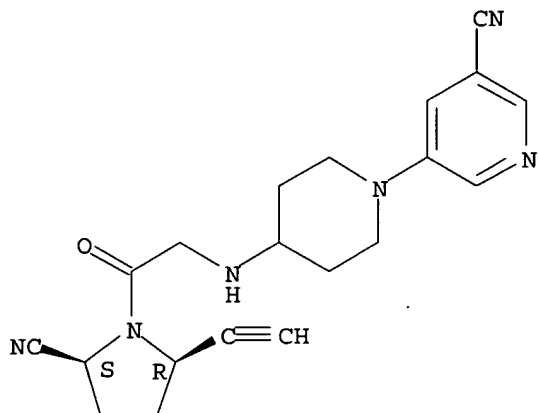
Absolute stereochemistry.



RN 676559-76-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-3-pyridinyl)-4-piperidinyl]amino]acetyl]-5-ethynyl-, hydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

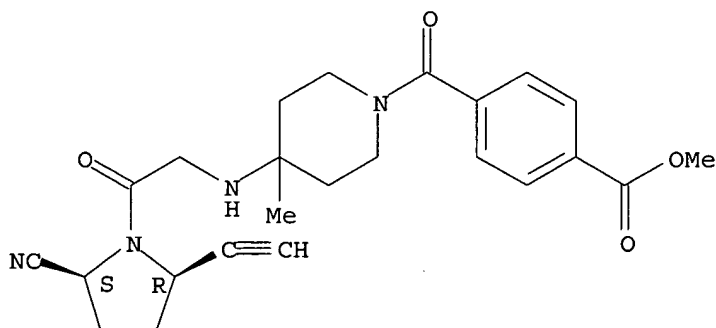


●x HCl

RN 676559-80-1 CAPLUS

CN Benzoic acid, 4-[[4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-4-methyl-1-piperidinyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

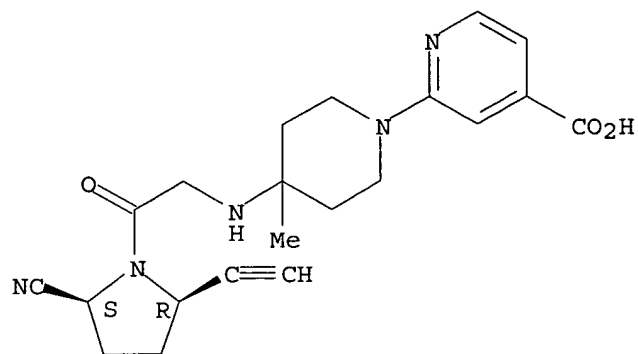
Absolute stereochemistry.



RN 676559-83-4 CAPLUS

CN 4-Pyridinecarboxylic acid, 2-[4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-4-methyl-1-piperidinyl]- (9CI) (CA INDEX NAME)

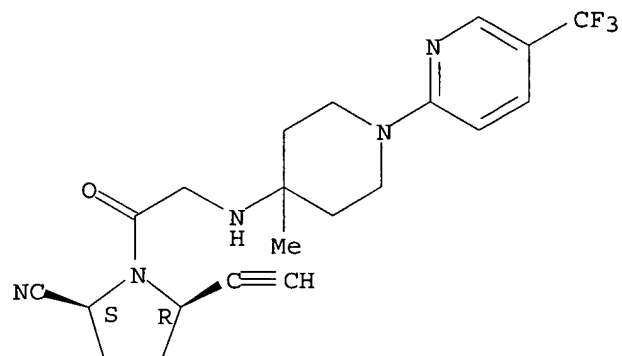
Absolute stereochemistry.



RN 676559-84-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[5-(trifluoromethyl)-2-pyridinyl]-4-piperidiny]amino]acetyl]-, hydrochloride, (2S,5R)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

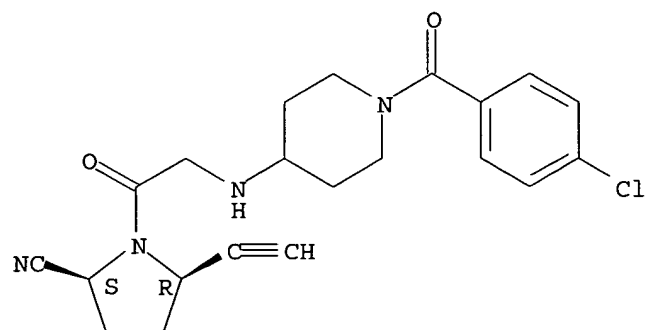


●x HCl

RN 676559-86-7 CAPLUS

CN 4-Piperidinamine, 1-(4-chlorobenzoyl)-N-[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

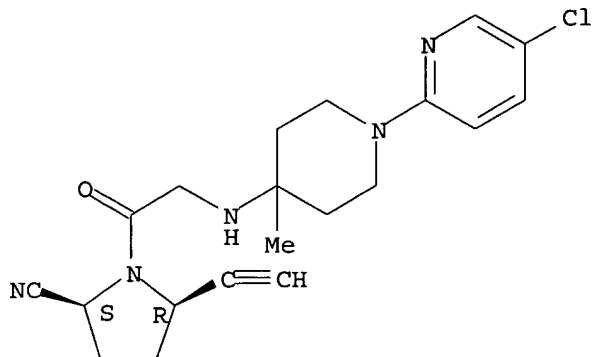
Absolute stereochemistry.



RN 676559-88-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-chloro-2-pyridinyl)-4-methyl-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676559-89-0 CAPLUS

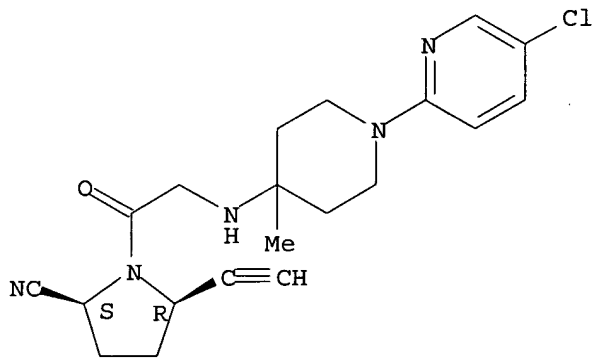
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-chloro-2-pyridinyl)-4-methyl-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 676559-88-9

CMF C20 H24 Cl N5 O

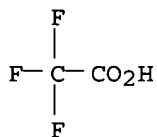
Absolute stereochemistry.



CM 2

CRN 76-05-1

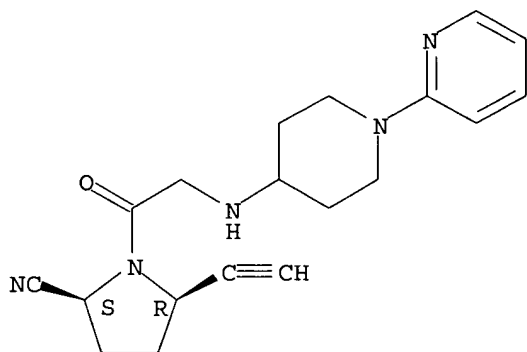
CMF C2 H F3 O2



RN 676559-91-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1-(2-pyridinyl)-4-piperidinyl]amino]acetyl]-, hydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

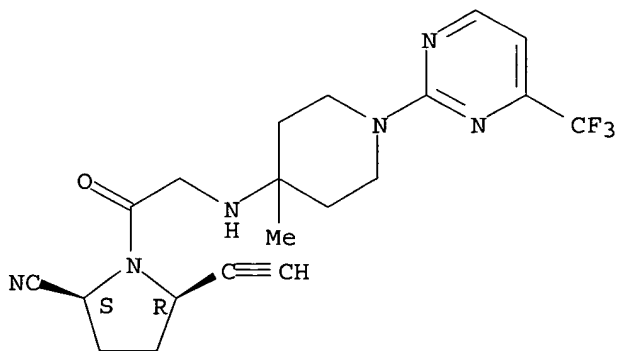


● x HCl

RN 676559-92-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[4-(trifluoromethyl)-2-pyrimidinyl]-4-piperidinyl]amino]acetyl]-, hydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

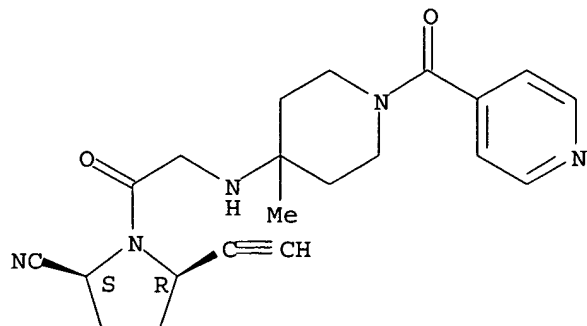


● x HCl

RN 676559-95-8 CAPLUS

CN 4-Piperidinamine, N-[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]-4-methyl-1-(4-pyridinylcarbonyl)-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

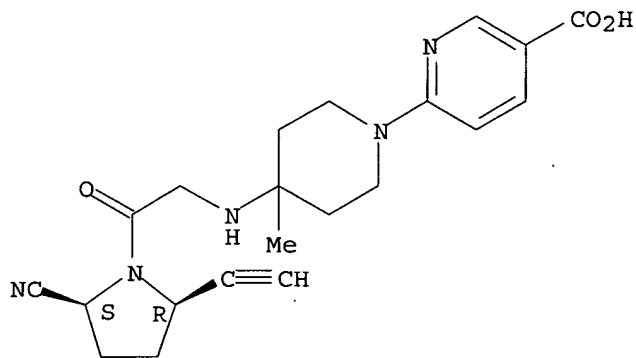


● x HCl

RN 676559-99-2 CAPLUS

CN 3-Pyridinecarboxylic acid, 6-[4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-4-methyl-1-piperidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676560-00-2 CAPLUS

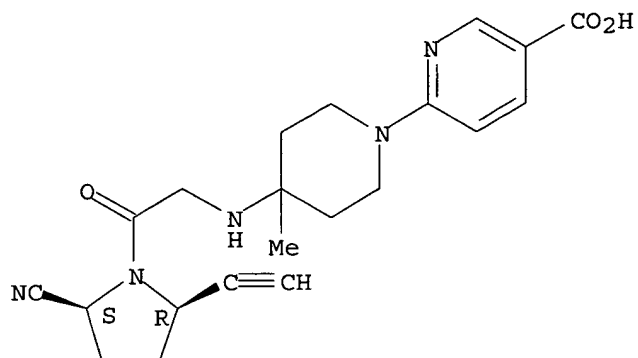
CN 3-Pyridinecarboxylic acid, 6-[4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-4-methyl-1-piperidinyl]-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 676559-99-2

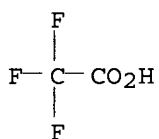
CMF C21 H25 N5 O3

Absolute stereochemistry.



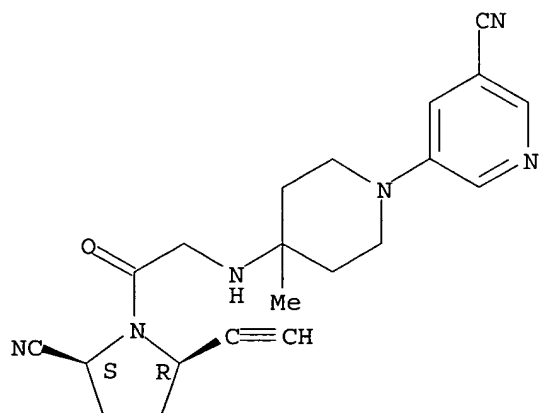
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 676560-04-6 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-3-pyridinyl)-4-methyl-4-piperidinyl]amino]acetyl]-5-ethynyl-, hydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

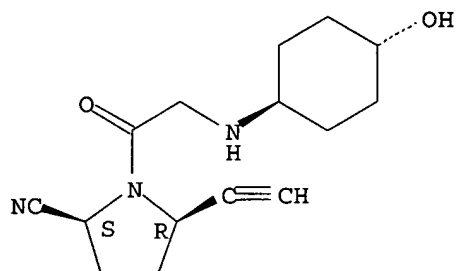


●x HCl

RN 676560-07-9 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-

hydroxycyclohexyl)amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

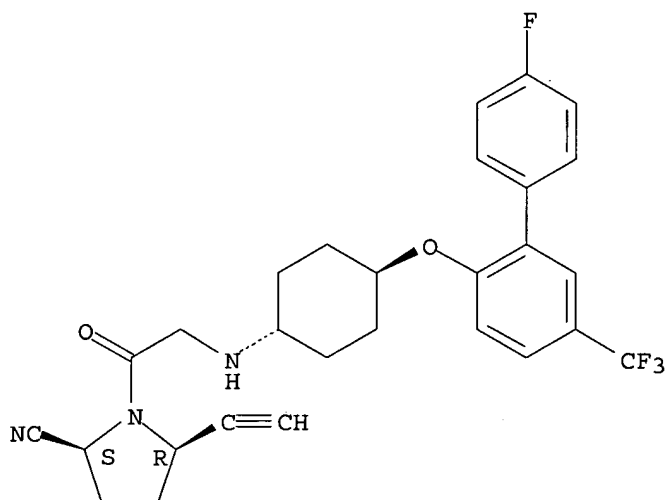
Absolute stereochemistry.



RN 676560-08-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[4'-fluoro-5-(trifluoromethyl)[1,1'-biphenyl]-2-yl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

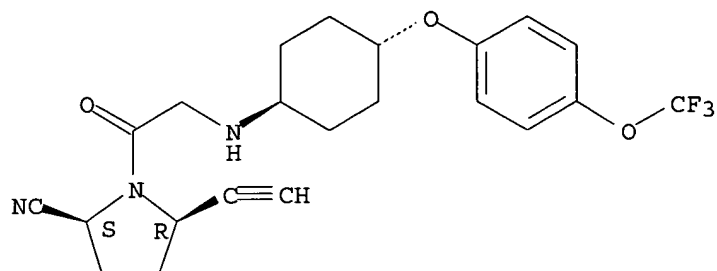
Absolute stereochemistry.



RN 676560-13-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[4-(trifluoromethoxy)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

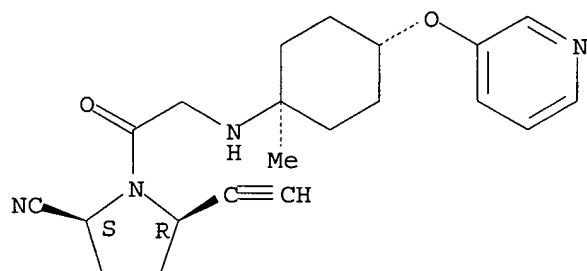
Absolute stereochemistry.



RN 676560-20-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-1-methyl-4-(3-pyridinyloxy)cyclohexyl]amino]acetyl]-, hydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

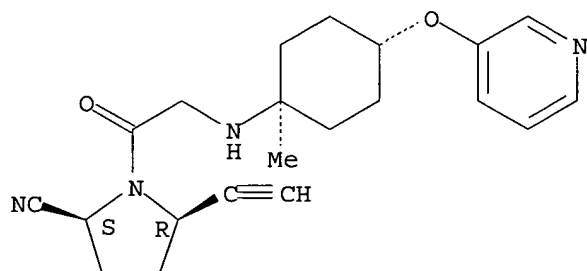


●x HCl

RN 676560-22-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-1-methyl-4-(3-pyridinyloxy)cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

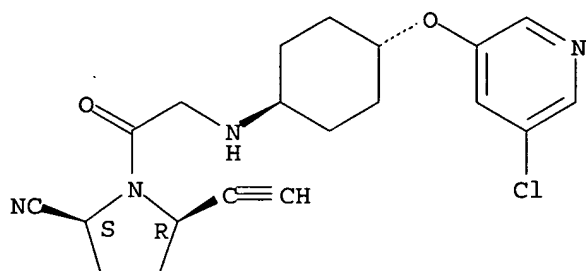
Absolute stereochemistry.



RN 676560-23-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(5-chloro-3-pyridinyl)oxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

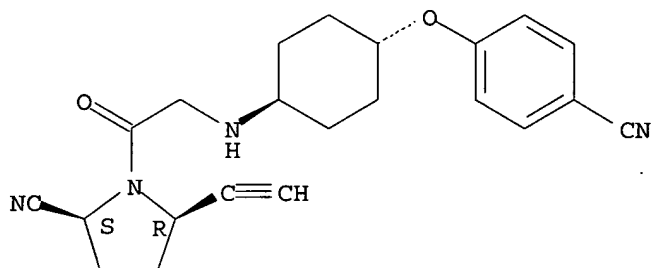
Absolute stereochemistry.



RN 676560-25-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(4-cyanophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

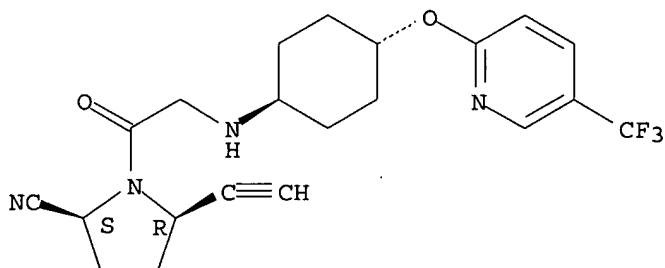
Absolute stereochemistry.



RN 676560-27-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[5-(trifluoromethyl)-2-pyridinyl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

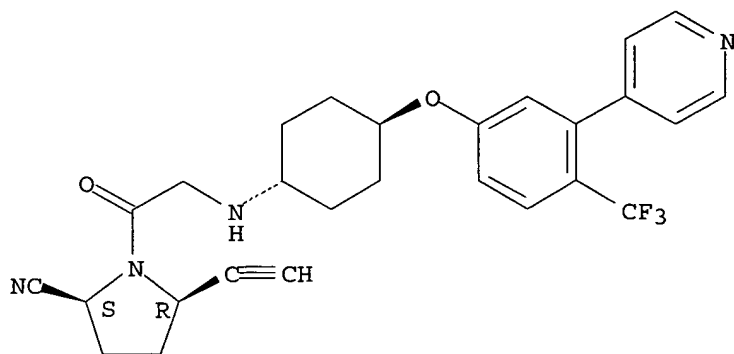
Absolute stereochemistry.



RN 676560-29-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[3-(4-pyridinyl)-4-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

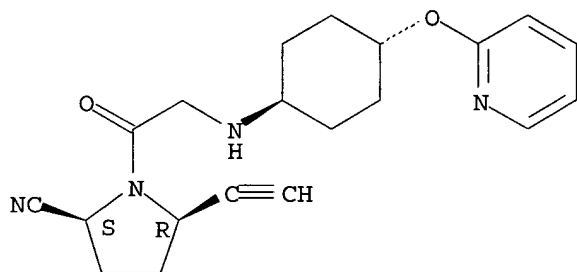
Absolute stereochemistry.



RN 676560-34-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-(2-pyridinyloxy)cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

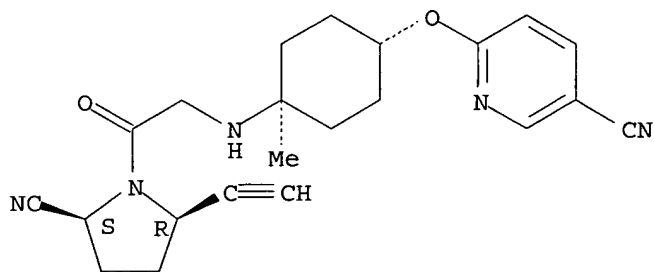
Absolute stereochemistry.



RN 676560-35-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(5-cyano-2-pyridinyl)oxy]-1-methylcyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

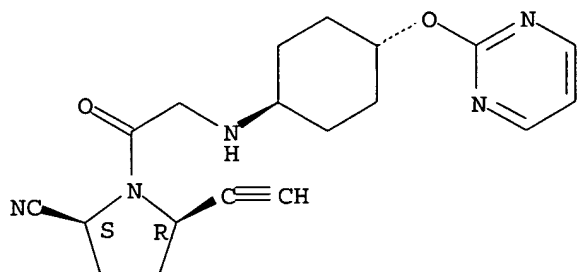
Absolute stereochemistry.



RN 676560-36-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-(2-pyrimidinyl)oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

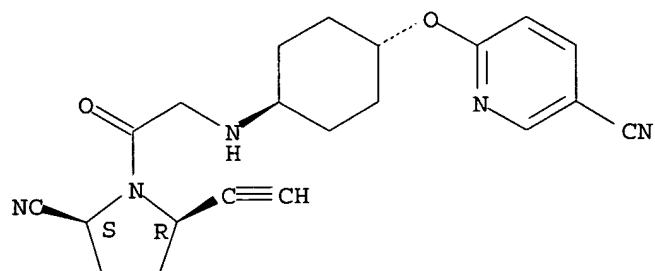
Absolute stereochemistry.



RN 676560-37-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(5-cyano-2-pyridinyl)oxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

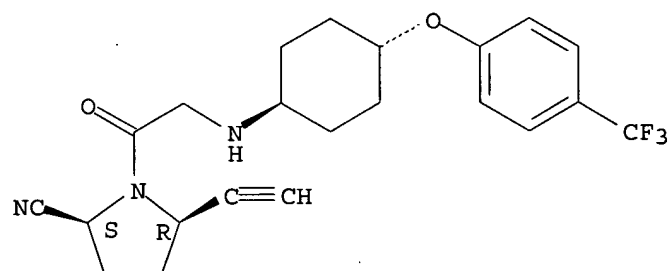
Absolute stereochemistry.



RN 676560-39-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[4-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

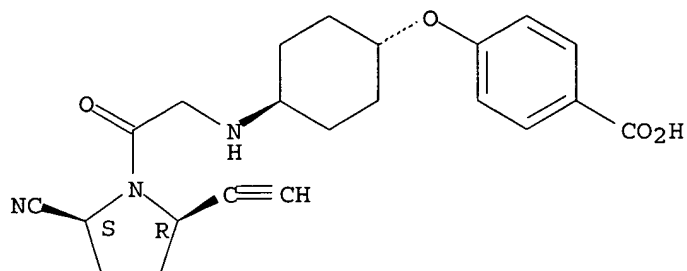
Absolute stereochemistry.



RN 676560-41-1 CAPLUS

CN Benzoic acid, 4-[[[trans-4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]cyclohexyl]oxy]- (9CI) (CA INDEX NAME)

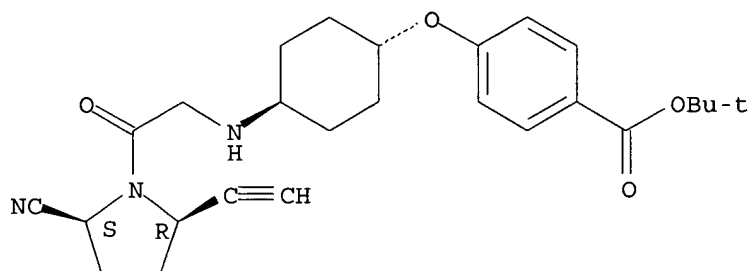
Absolute stereochemistry.



RN 676560-43-3 CAPLUS

CN Benzoic acid, 4-[[[trans-4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]cyclohexyl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

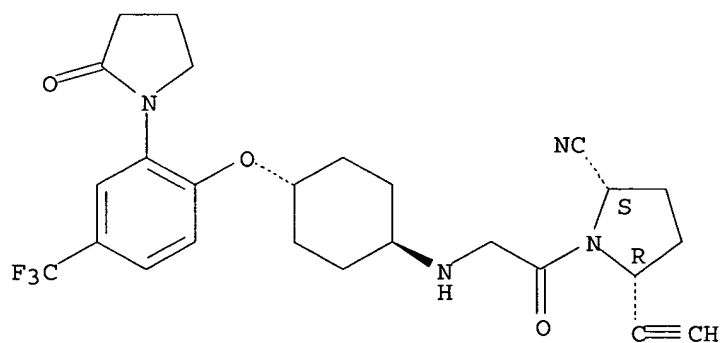
Absolute stereochemistry.



RN 676560-44-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[2-(2-oxo-1-pyrrolidinyl)-4-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

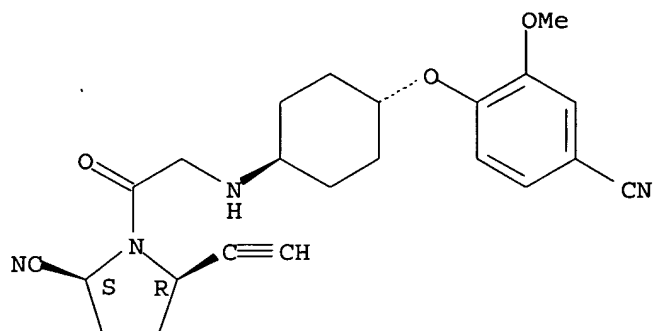
Absolute stereochemistry.



RN 676560-47-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(4-cyano-2-methoxyphenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

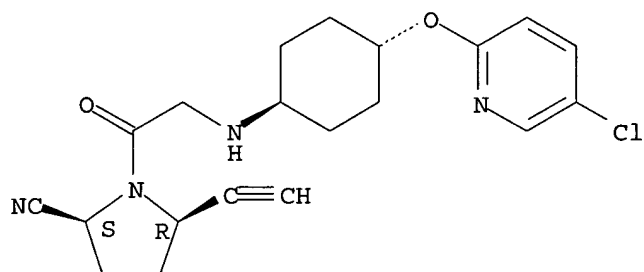
Absolute stereochemistry.



RN 676560-50-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(5-chloro-2-pyridinyl)oxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

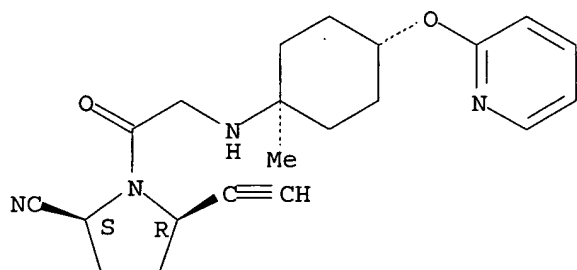
Absolute stereochemistry.



RN 676560-52-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-1-methyl-4-(2-pyridinyloxy)cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

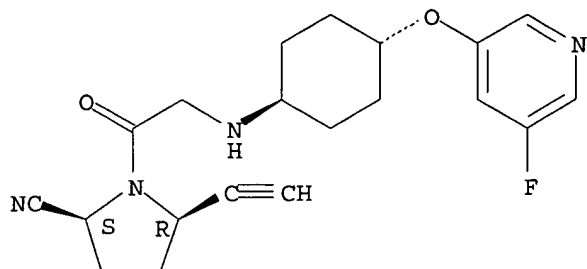
Absolute stereochemistry.



RN 676560-54-6 CAPLUS

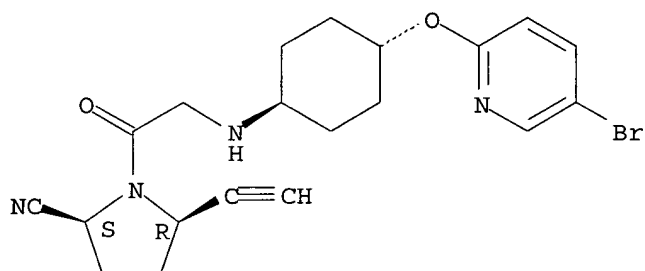
CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[(5-fluoro-3-pyridinyl)oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



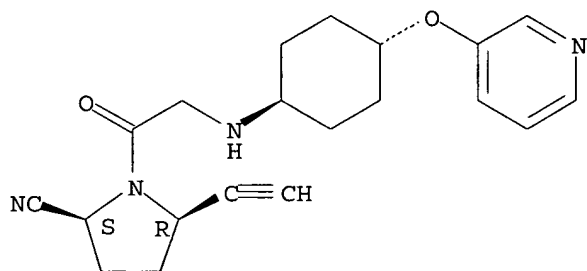
RN 676560-56-8 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[(5-bromo-2-pyridinyl)oxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



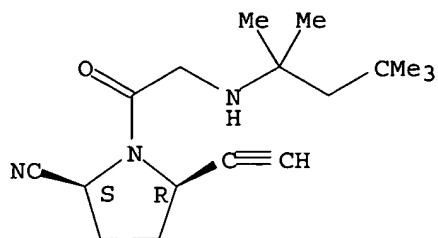
RN 676560-58-0 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-(3-pyridinyloxy)cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676560-60-4 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-(3-pyridinyloxy)cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

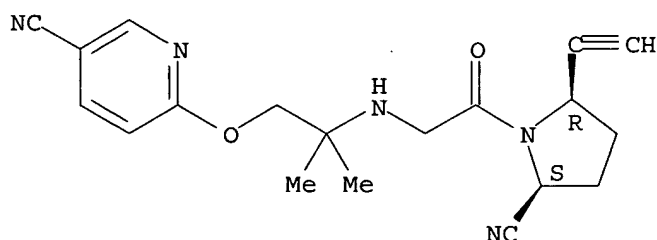
Absolute stereochemistry.



RN 676560-61-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(5-cyano-2-pyridinyl)oxy]-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

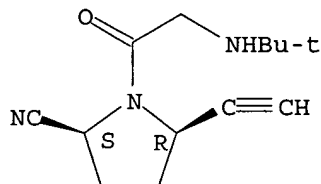
Absolute stereochemistry.



RN 676560-64-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

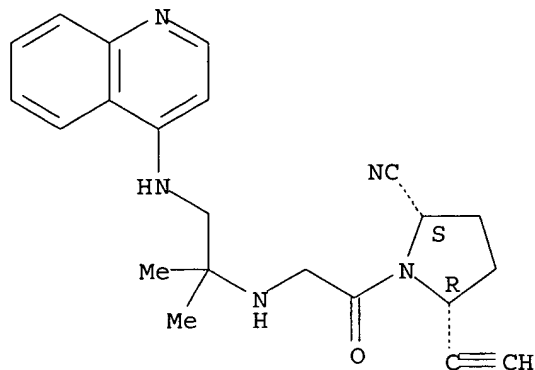


● HCl

RN 676560-65-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1,1-dimethyl-2-(4-quinolinylamino)ethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

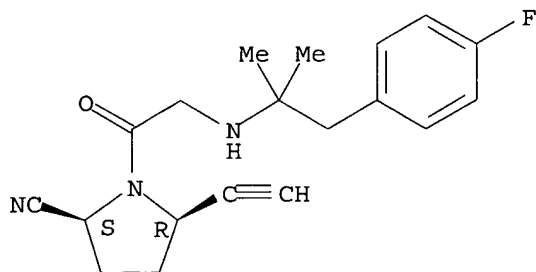
Absolute stereochemistry.



RN 676560-66-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[2-(4-fluorophenyl)-1,1-dimethylethyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

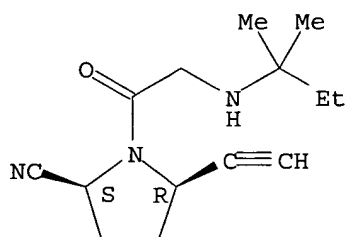
Absolute stereochemistry.



RN 676560-67-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(1,1-dimethylpropyl)amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

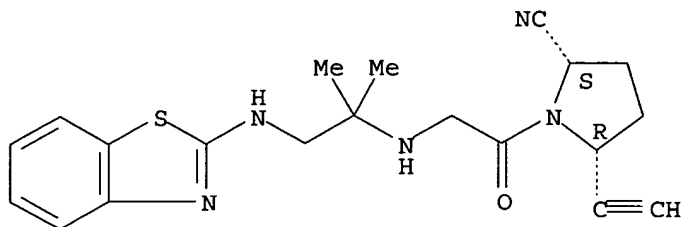
Absolute stereochemistry.



RN 676560-68-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-(2-benzothiazolylamino)-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

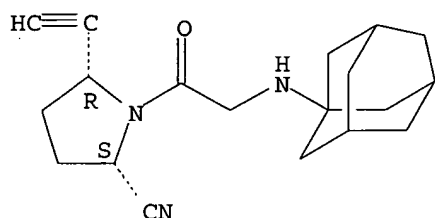
Absolute stereochemistry.



RN 676560-69-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[(tricyclo[3.3.1.1.3,7]dec-1-ylamino)acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

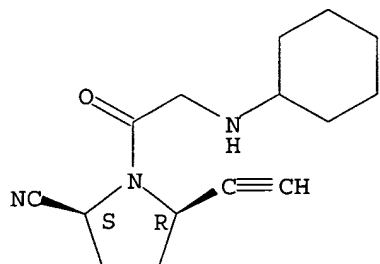
Absolute stereochemistry.



RN 676560-70-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclohexylamino)acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

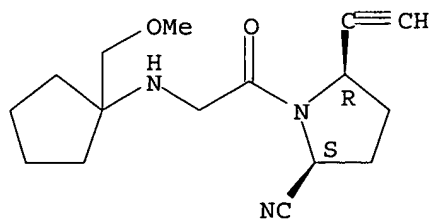
Absolute stereochemistry.



RN 676560-71-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1-(methoxymethyl)cyclopentyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

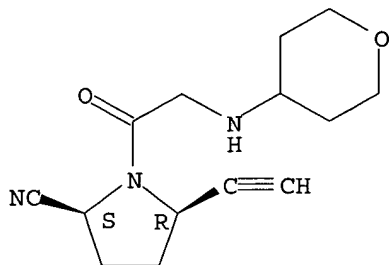
Absolute stereochemistry.



RN 676560-75-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(tetrahydro-2H-pyran-4-yl)amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

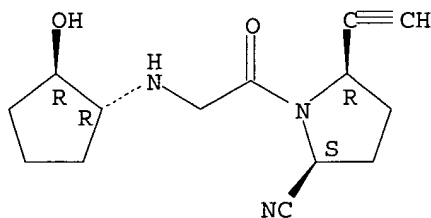
Absolute stereochemistry.



RN 676560-76-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(1R,2R)-2-hydroxycyclopentyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

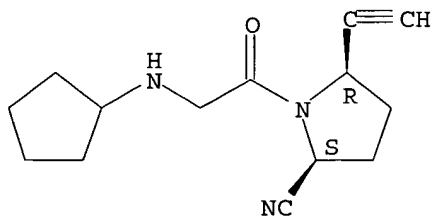
Absolute stereochemistry.



RN 676560-77-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclopentylamino)acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

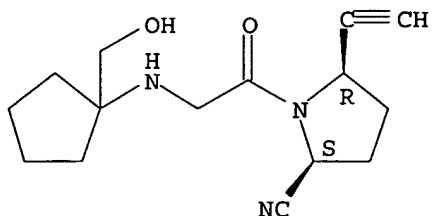
Absolute stereochemistry.



RN 676560-79-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1-(hydroxymethyl)cyclopentyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

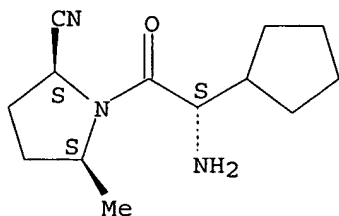
Absolute stereochemistry.



RN 676560-81-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclopentylacetyl]-5-methyl-, (2S,5S)-(9CI) (CA INDEX NAME)

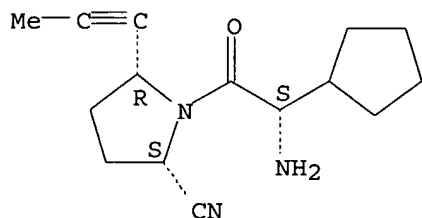
Absolute stereochemistry.



RN 676560-90-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclopentylacetyl]-5-(1-propynyl)-, (2S,5R)-(9CI) (CA INDEX NAME)

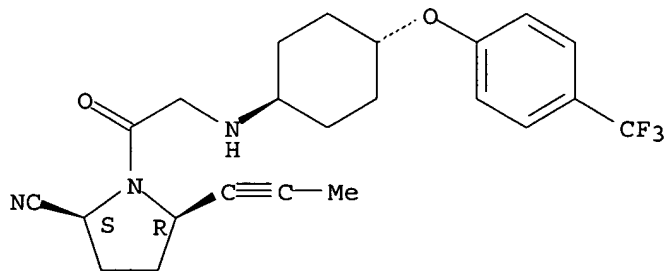
Absolute stereochemistry.



RN 676560-97-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-(1-propynyl)-1-[[[trans-4-[4-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)-(9CI) (CA INDEX NAME)

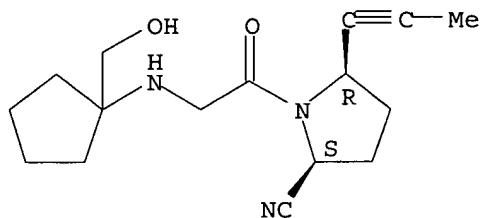
Absolute stereochemistry.



RN 676560-99-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(hydroxymethyl)cyclopentyl]amino]acetyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

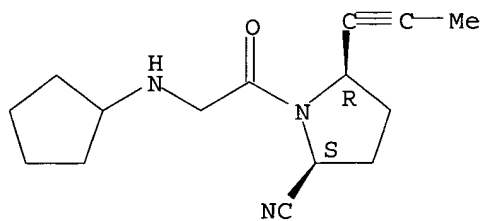
Absolute stereochemistry.



RN 676561-00-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclopentylamino)acetyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

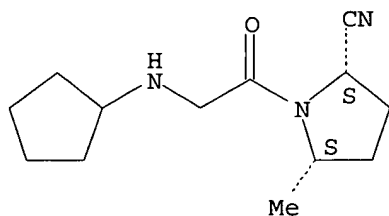
Absolute stereochemistry.



RN 676561-04-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclopentylamino)acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

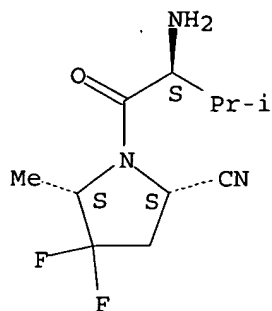
Absolute stereochemistry.



RN 676561-07-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3-methyl-1-oxobutyl]-4,4-difluoro-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

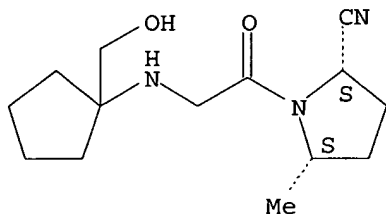
Absolute stereochemistry.



RN 676561-09-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(hydroxymethyl)cyclopentyl]amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

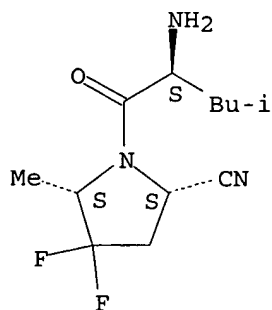
Absolute stereochemistry.



RN 676561-10-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-4,4-difluoro-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

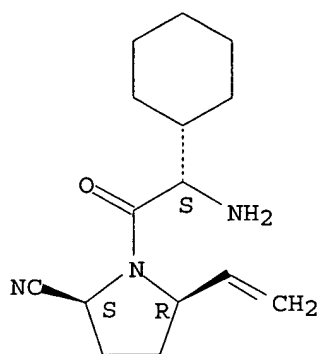
Absolute stereochemistry.



RN 676561-20-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclohexylacetyl]-5-ethenyl-, (2S,5R)- (9CI) (CA INDEX NAME)

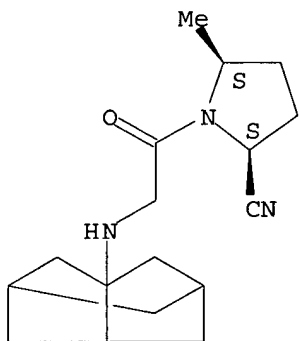
Absolute stereochemistry.



RN 676561-26-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(hexahydro-2,5-methanopentalen-3a(1H)-yl)amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

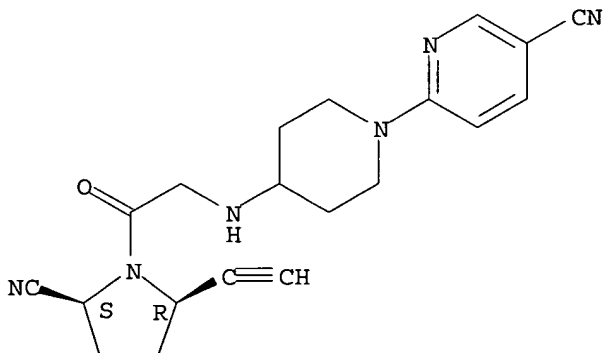
Absolute stereochemistry.



RN 676561-28-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-2-pyridinyl)-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

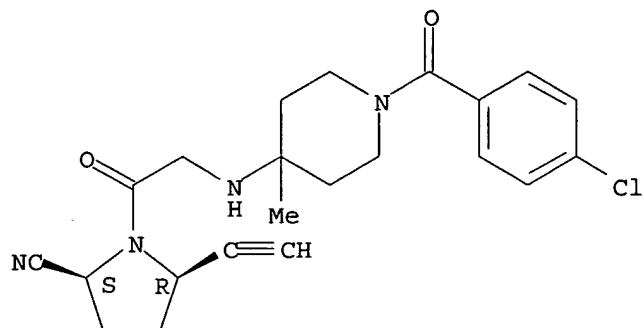
Absolute stereochemistry.



RN 676561-29-8 CAPLUS

CN 4-Piperidinamine, 1-(4-chlorobenzoyl)-N-[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]-4-methyl-, (9CI) (CA INDEX NAME)

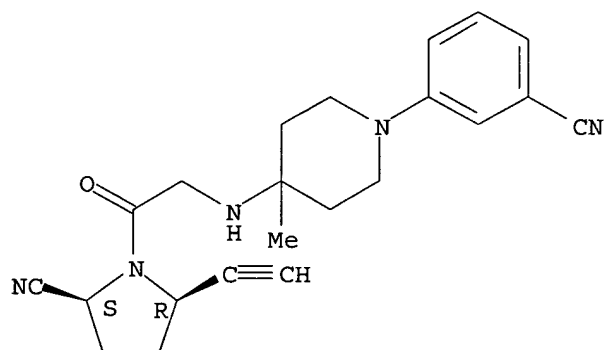
Absolute stereochemistry.



RN 676561-30-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(3-cyanophenyl)-4-methyl-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

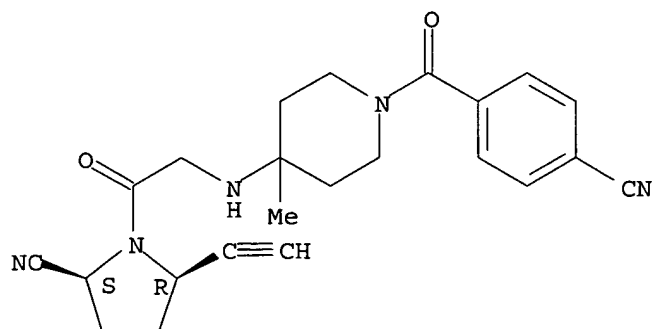
Absolute stereochemistry.



RN 676561-31-2 CAPLUS

CN 4-Piperidinamine, 1-(4-cyanobenzoyl)-N-[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]-4-methyl- (9CI) (CA INDEX NAME)

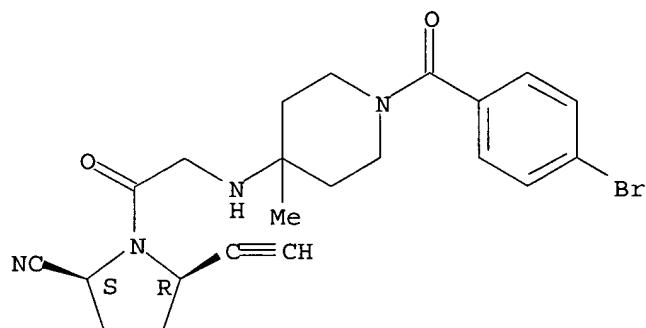
Absolute stereochemistry.



RN 676561-32-3 CAPLUS

CN 4-Piperidinamine, 1-(4-bromobenzoyl)-N-[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]-4-methyl- (9CI) (CA INDEX NAME)

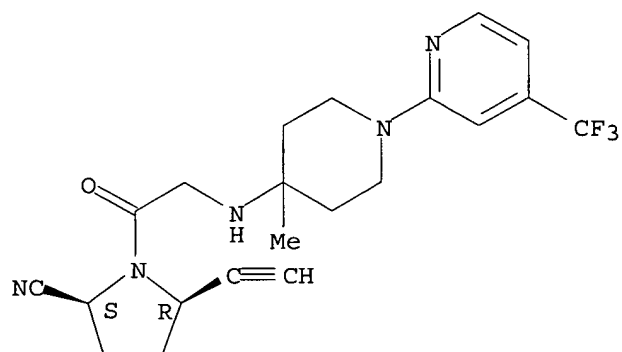
Absolute stereochemistry.



RN 676561-33-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[4-(trifluoromethyl)-2-pyridinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

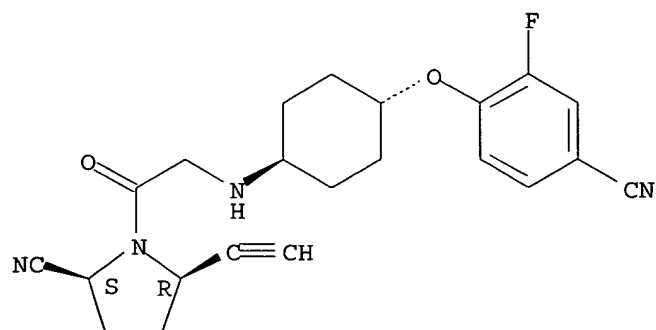
Absolute stereochemistry.



RN 676561-34-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(4-cyano-2-fluorophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

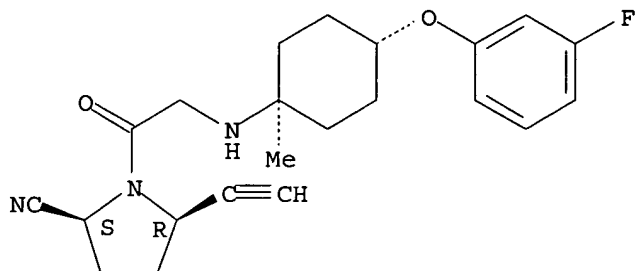
Absolute stereochemistry.



RN 676561-35-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-(3-fluorophenoxy)-1-methylcyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

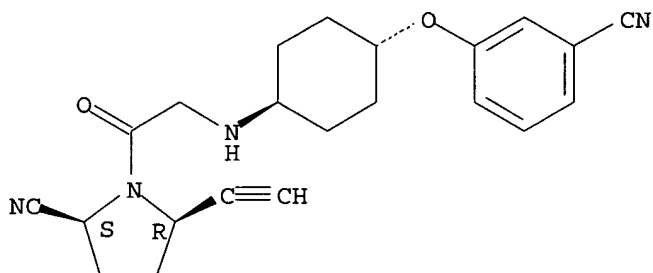
Absolute stereochemistry.



RN 676561-36-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(3-cyanophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

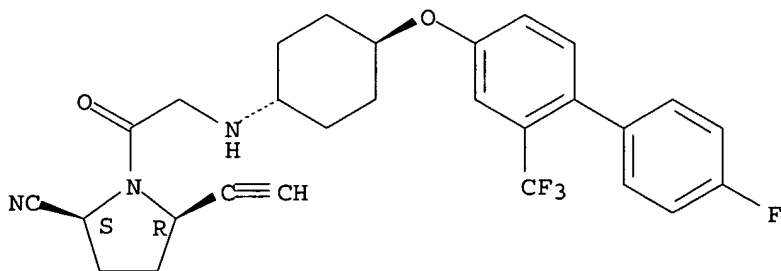
Absolute stereochemistry.



RN 676561-37-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[4'-fluoro-2-(trifluoromethyl)[1,1'-biphenyl]-4-yl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

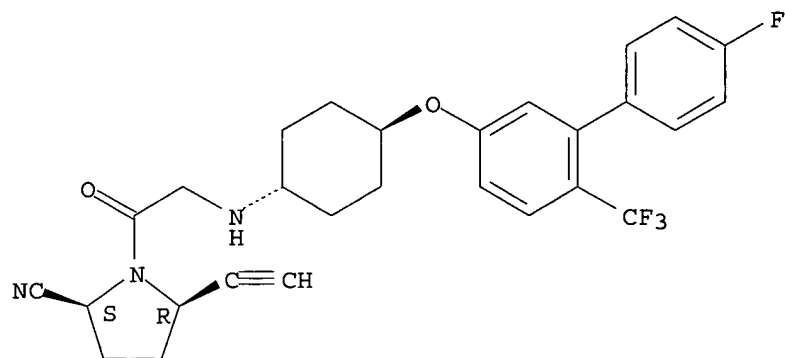
Absolute stereochemistry.



RN 676561-38-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[4'-fluoro-6-(trifluoromethyl)[1,1'-biphenyl]-3-yl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

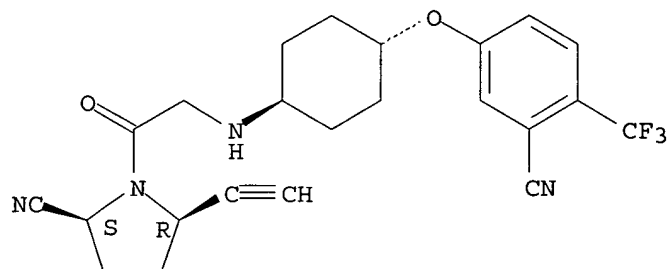
Absolute stereochemistry.



RN 676561-39-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[3-cyano-4-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

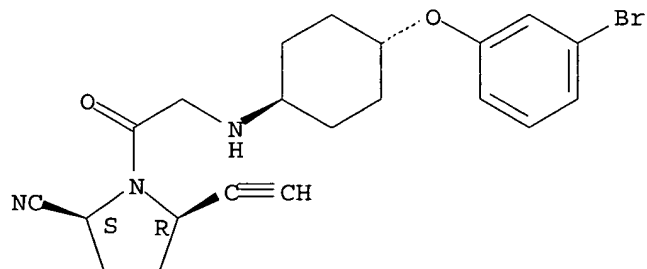
Absolute stereochemistry.



RN 676561-40-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(3-bromophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

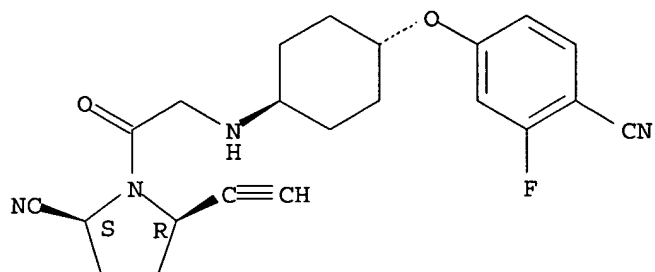
Absolute stereochemistry.



RN 676561-41-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(4-cyano-3-fluorophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

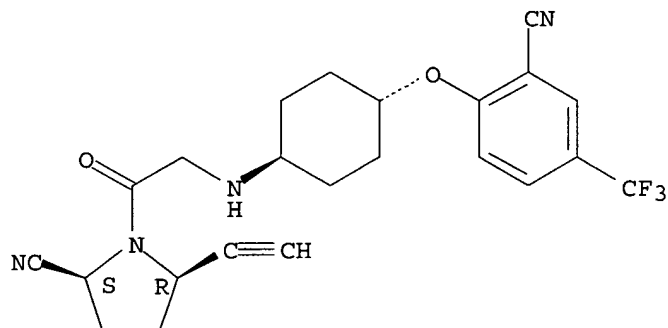
Absolute stereochemistry.



RN 676561-42-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[2-cyano-4-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

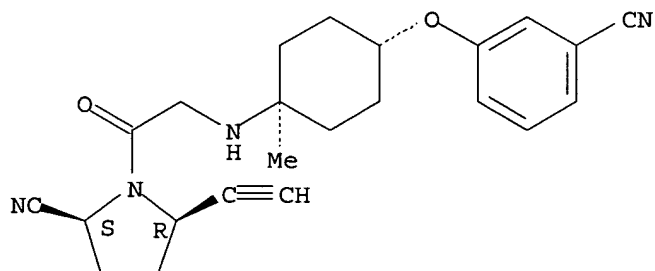
Absolute stereochemistry.



RN 676561-43-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(3-cyanophenoxy)-1-methylcyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

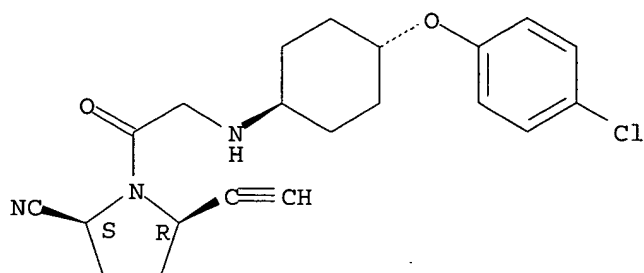
Absolute stereochemistry.



RN 676561-44-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(4-chlorophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

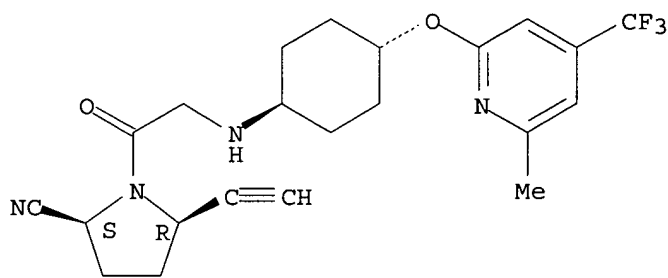
Absolute stereochemistry.



RN 676561-45-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[6-methyl-4-(trifluoromethyl)-2-pyridinyl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)-(9CI) (CA INDEX NAME)

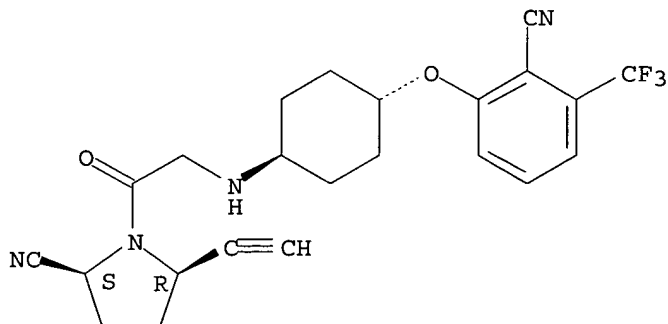
Absolute stereochemistry.



RN 676561-46-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[2-cyano-3-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)-(9CI) (CA INDEX NAME)

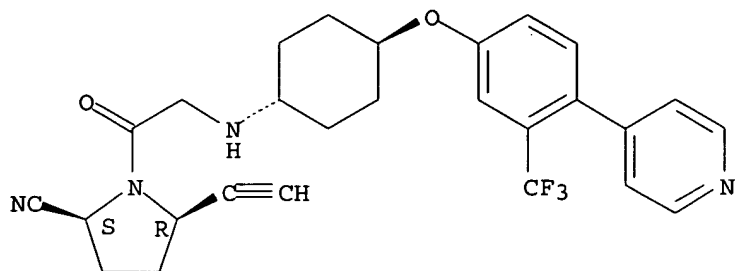
Absolute stereochemistry.



RN 676561-47-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[4-(4-pyridinyl)-3-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)-(9CI) (CA INDEX NAME)

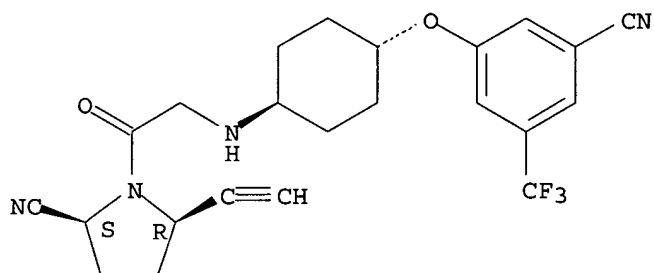
Absolute stereochemistry.



RN 676561-48-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[3-cyano-5-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

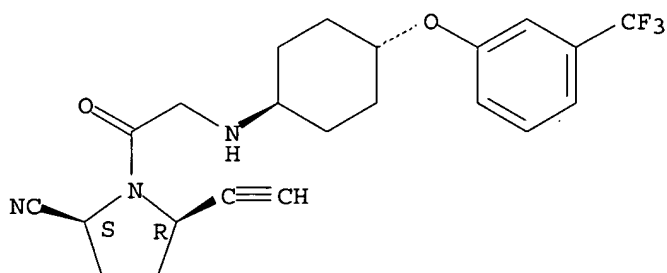
Absolute stereochemistry.



RN 676561-49-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[3-(trifluoromethyl)phenoxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

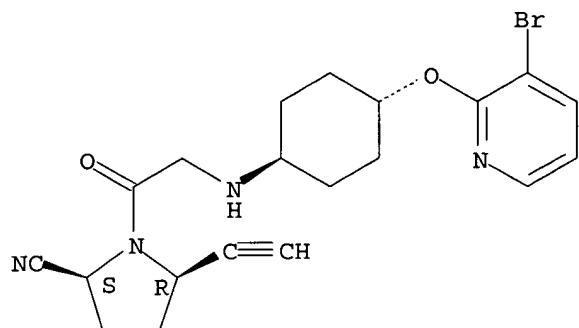
Absolute stereochemistry.



RN 676561-50-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[3-(3-bromo-2-pyridinyl)oxy]cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

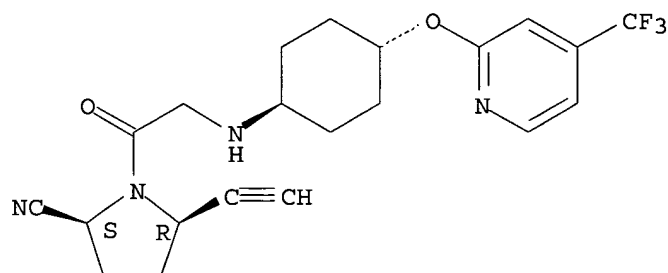
Absolute stereochemistry.



RN 676561-51-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-4-[[4-(trifluoromethyl)-2-pyridinyl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

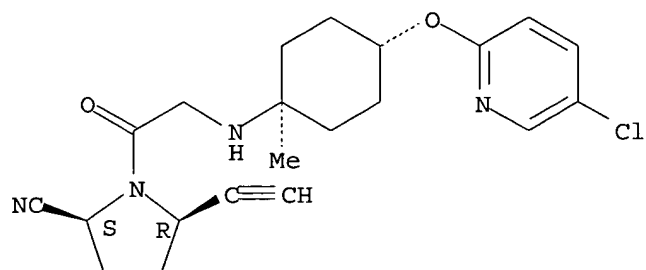
Absolute stereochemistry.



RN 676561-52-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-[[5-chloro-2-pyridinyl]oxy]-1-methylcyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

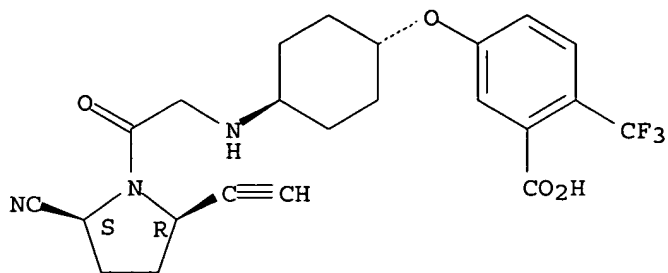
Absolute stereochemistry.



RN 676561-53-8 CAPLUS

CN Benzoic acid, 5-[[[trans-4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]cyclohexyl]oxy]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

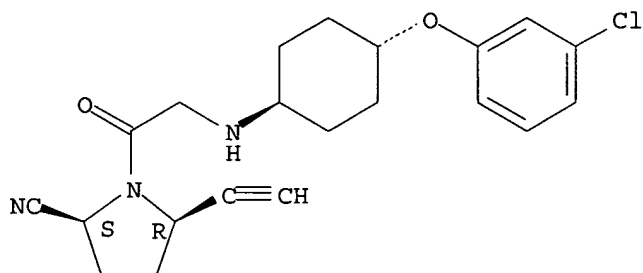
Absolute stereochemistry.



RN 676561-54-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(3-chlorophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

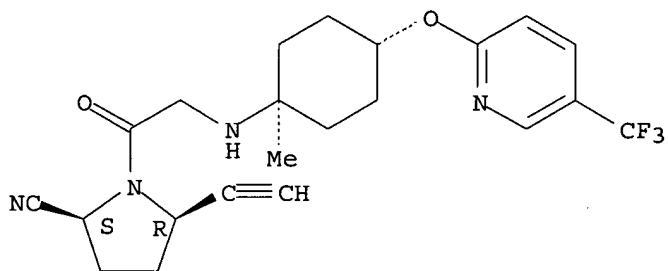
Absolute stereochemistry.



RN 676561-55-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[trans-1-methyl-4-[[5-(trifluoromethyl)-2-pyridinyl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

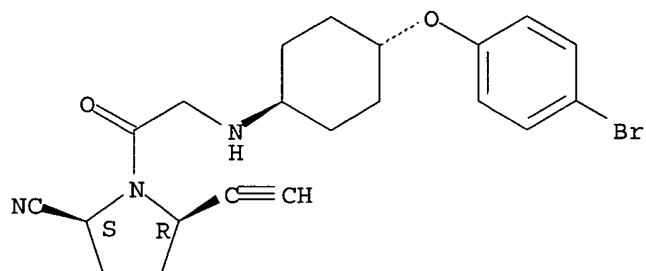
Absolute stereochemistry.



RN 676561-56-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[trans-4-(4-bromophenoxy)cyclohexyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

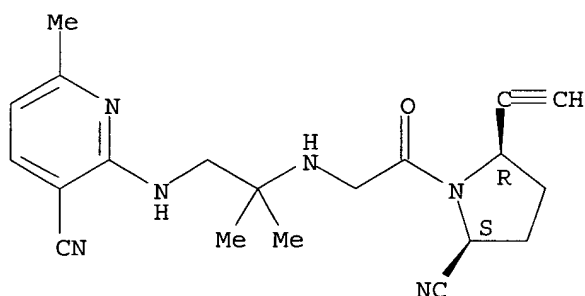
Absolute stereochemistry.



RN 676561-57-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(3-cyano-6-methyl-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

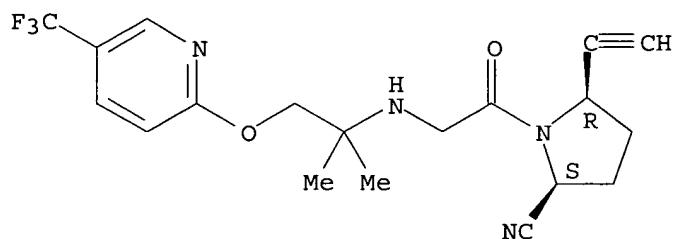
Absolute stereochemistry.



RN 676561-58-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1,1-dimethyl-2-[[5-(trifluoromethyl)-2-pyridinyl]oxy]ethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

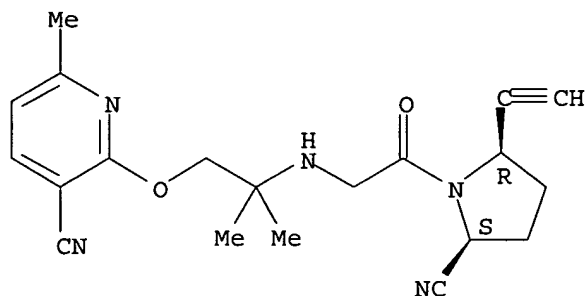
Absolute stereochemistry.



RN 676561-59-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(3-cyano-6-methyl-2-pyridinyl)oxy]-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

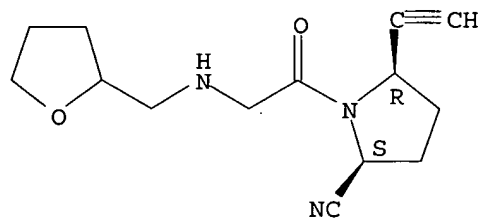
Absolute stereochemistry.



RN 676561-60-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[2-(4-cyanophenyl)ethyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

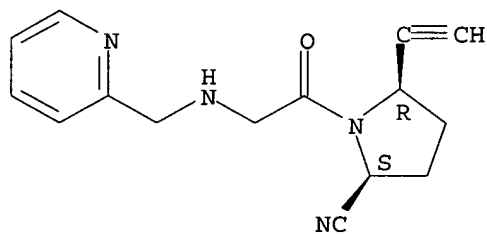
Absolute stereochemistry.



RN 676561-61-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[2-(2-pyridinylmethyl)amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

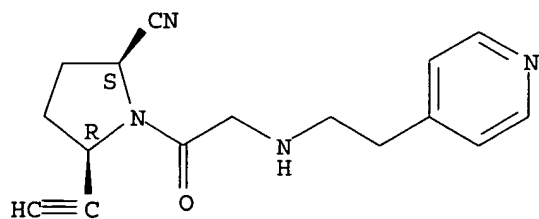
Absolute stereochemistry.



RN 676561-62-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[2-(4-pyridinyl)ethyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

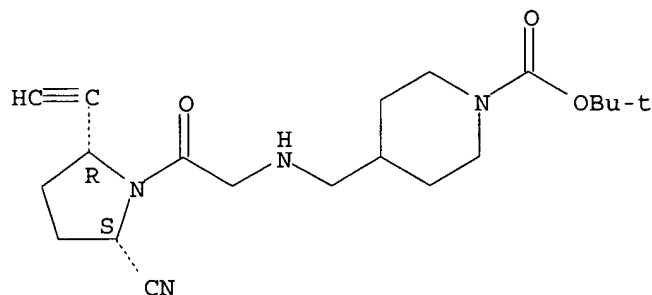
Absolute stereochemistry.



RN 676561-63-0 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]methyl]-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)

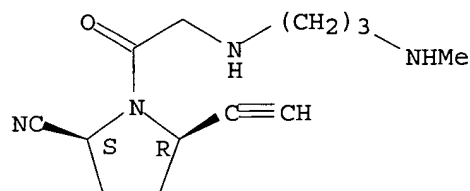
Absolute stereochemistry.



RN 676561-64-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[3-(methylamino)propyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

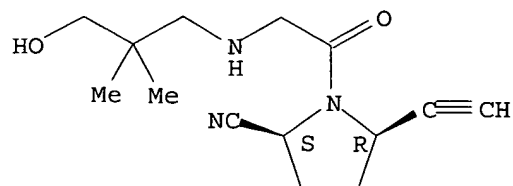
Absolute stereochemistry.



RN 676561-66-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[3-hydroxy-2,2-dimethylpropyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

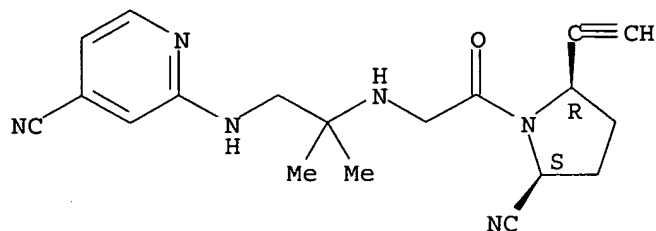
Absolute stereochemistry.



RN 676561-67-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(4-cyano-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

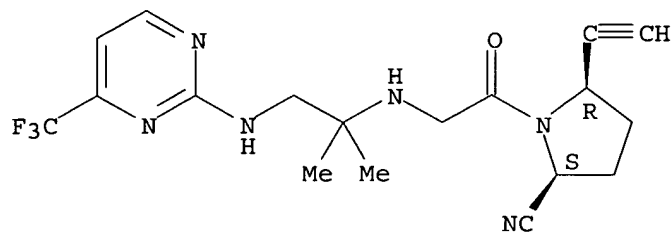
Absolute stereochemistry.



RN 676561-68-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1,1-dimethyl-2-[[4-(trifluoromethyl)-2-pyrimidinyl]amino]ethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

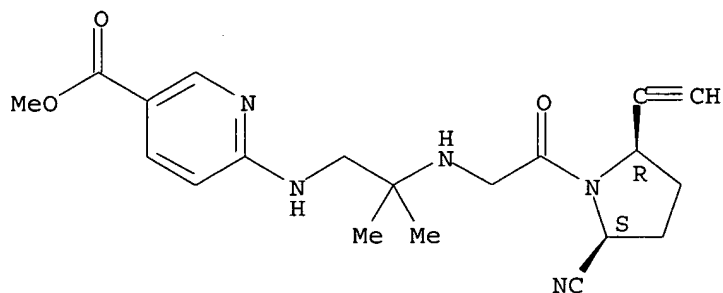
Absolute stereochemistry.



RN 676561-69-6 CAPLUS

CN 3-Pyridinecarboxylic acid, 6-[[2-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-2-methylpropyl]amino]-, methyl ester (9CI) (CA INDEX NAME)

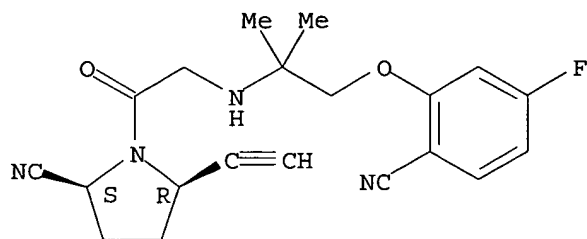
Absolute stereochemistry.



RN 676561-70-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-(2-cyano-5-fluorophenoxy)-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

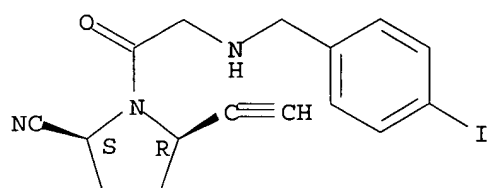
Absolute stereochemistry.



RN 676561-71-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(4-iodophenyl)methyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

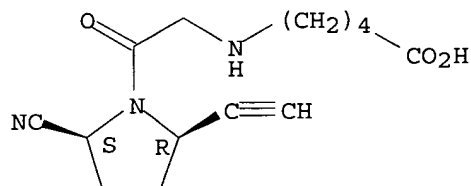
Absolute stereochemistry.



RN 676561-73-2 CAPLUS

CN Pentanoic acid, 5-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]- (9CI) (CA INDEX NAME)

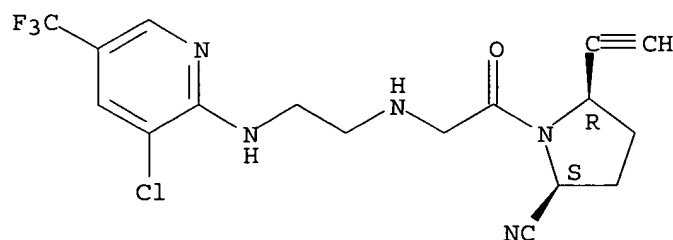
Absolute stereochemistry.



RN 676561-74-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]amino]ethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

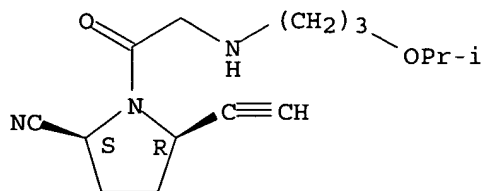
Absolute stereochemistry.



RN 676561-75-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[3-(1-methylethoxy)propyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

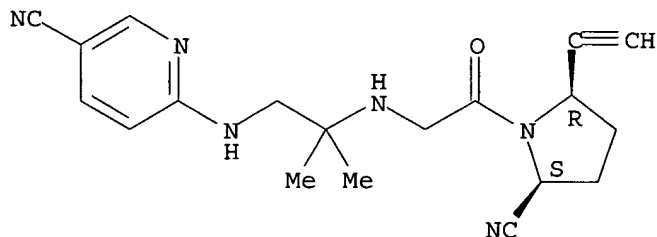
Absolute stereochemistry.



RN 676561-76-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(5-cyano-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

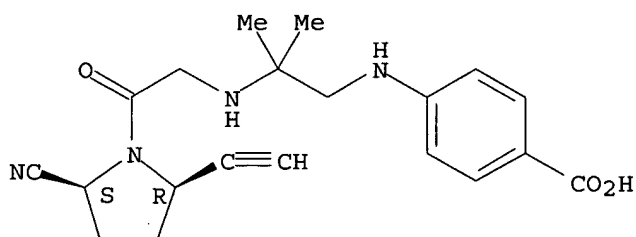
Absolute stereochemistry.



RN 676561-78-7 CAPLUS

CN Benzoic acid, 4-[[[2-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-2-methylpropyl]amino]-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

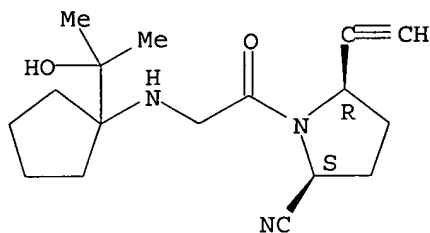


●x HCl

RN 676561-79-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1-(1-hydroxy-1-methylethyl)cyclopentyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

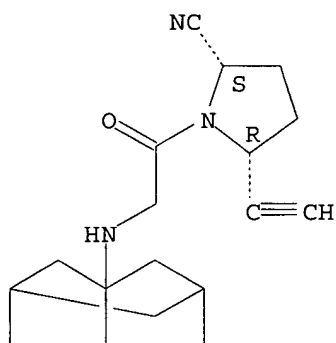
Absolute stereochemistry.



RN 676561-81-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[hexahydro-2,5-methanopentalen-3a(1H)-yl]amino]acetyl-, (2S,5R)- (9CI) (CA INDEX NAME)

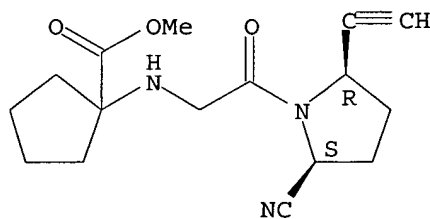
Absolute stereochemistry.



RN 676561-82-3 CAPLUS

CN Cyclopentanecarboxylic acid, 1-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-, methyl ester (9CI) (CA INDEX NAME)

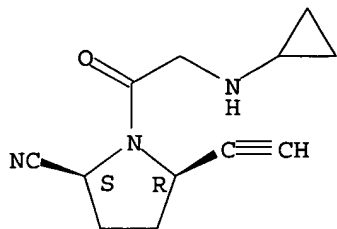
Absolute stereochemistry.



RN 676561-83-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclopropylamino)acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

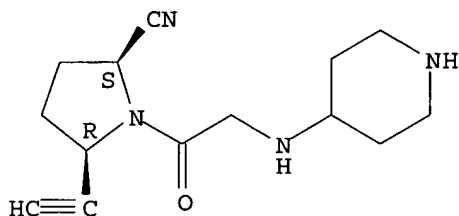
Absolute stereochemistry.



RN 676561-84-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[(4-piperidinylamino)acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

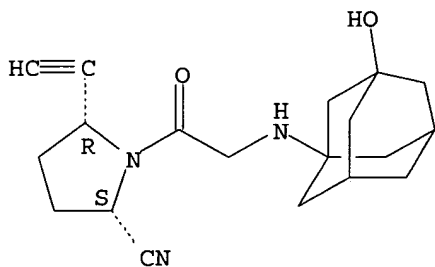
Absolute stereochemistry.



RN 676561-85-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[3-hydroxytricyclo[3.3.1.1.3,7]dec-1-yl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

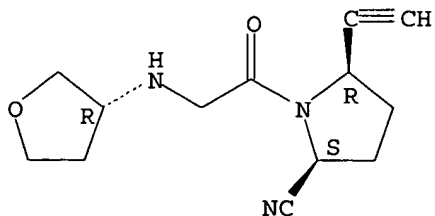
Absolute stereochemistry.



RN 676561-86-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(3R)-tetrahydro-3-furanyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

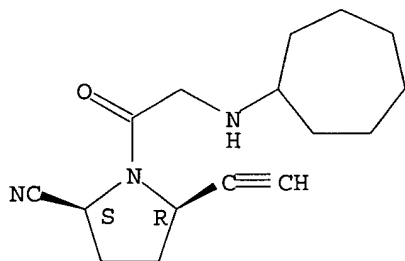
Absolute stereochemistry.



RN 676561-87-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cycloheptylamino)acetyl]-5-ethynyl-,
(2S,5R)- (9CI) (CA INDEX NAME)

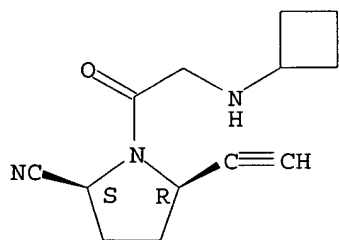
Absolute stereochemistry.



RN 676561-88-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclobutylamino)acetyl]-5-ethynyl-,
(2S,5R)- (9CI) (CA INDEX NAME)

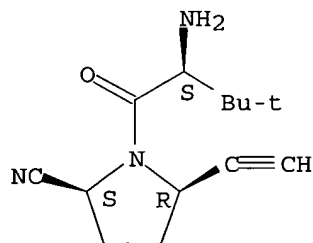
Absolute stereochemistry.



RN 676561-89-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

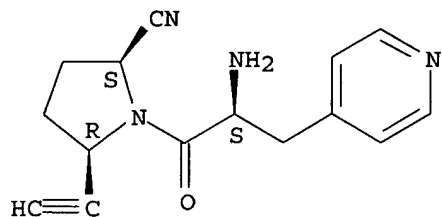
Absolute stereochemistry.



RN 676561-90-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-1-oxo-3-(4-pyridinyl)propyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

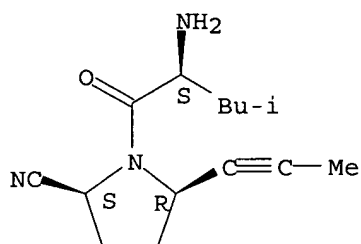
Absolute stereochemistry.



RN 676561-92-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

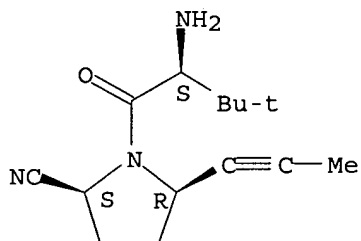
Absolute stereochemistry.



RN 676561-93-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

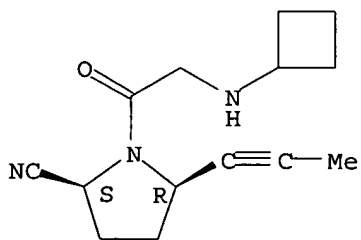
Absolute stereochemistry.



RN 676561-94-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(cyclobutylamino)acetyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

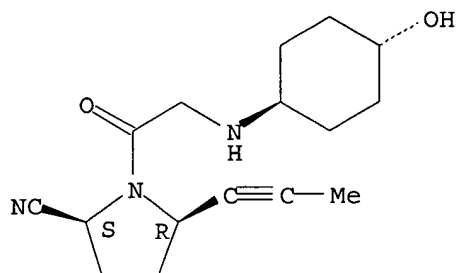
Absolute stereochemistry.



RN 676561-95-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(trans-4-hydroxycyclohexyl)amino]acetyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

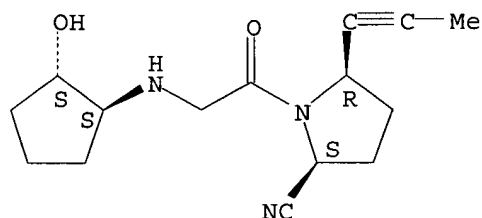
Absolute stereochemistry.



RN 676561-96-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(1S,2S)-2-hydroxycyclopentyl]amino]acetyl]-5-(1-propynyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

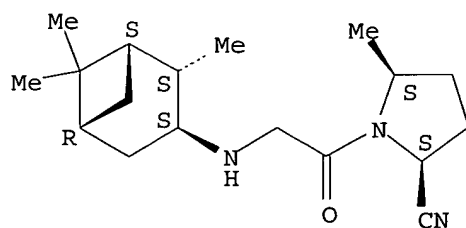
Absolute stereochemistry.



RN 676561-97-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-methyl-1-[[[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino]acetyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

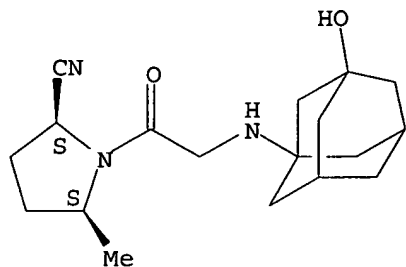
Absolute stereochemistry.



RN 676561-98-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-hydroxytricyclo[3.3.1.1.3,7]dec-1-yl)amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

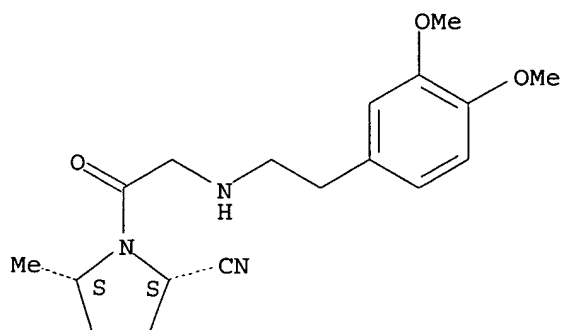
Absolute stereochemistry.



RN 676561-99-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-(3,4-dimethoxyphenyl)ethyl]amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

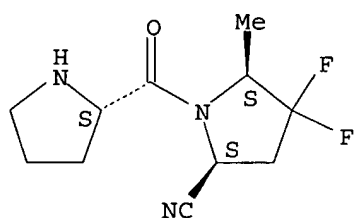
Absolute stereochemistry.



RN 676562-00-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-5-methyl-1-[(2S)-2-pyrrolidinylcarbonyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

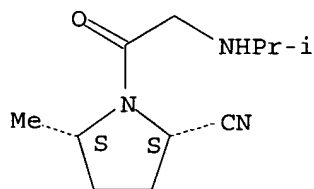
Absolute stereochemistry.



RN 676562-02-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-methyl-1-[[[1-methylethyl]amino]acetyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

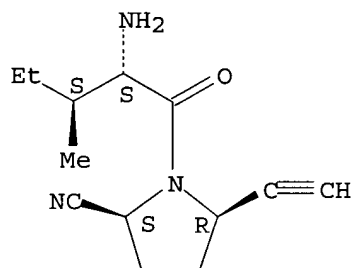
Absolute stereochemistry.



RN 676562-03-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

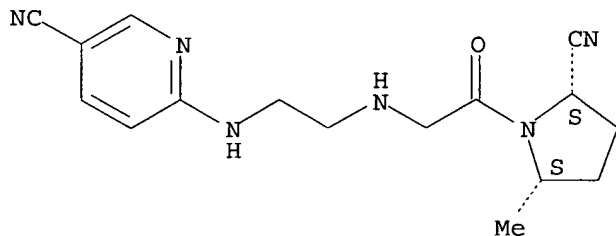
Absolute stereochemistry.



RN 676562-04-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(5-cyano-2-pyridinyl)amino]ethyl]amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

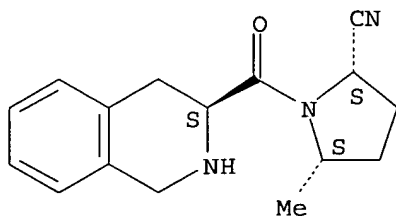
Absolute stereochemistry.



RN 676562-05-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-methyl-1-[[[(3S)-1,2,3,4-tetrahydro-3-isoquinolinyl]carbonyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

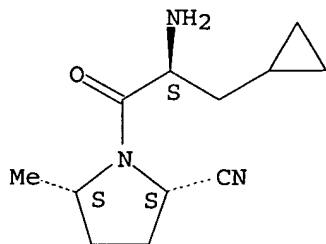
Absolute stereochemistry.



RN 676562-06-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3-cyclopropyl-1-oxopropyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

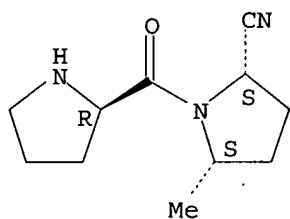
Absolute stereochemistry.



RN 676562-07-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-methyl-1-[(2R)-2-pyrrolidinylcarbonyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

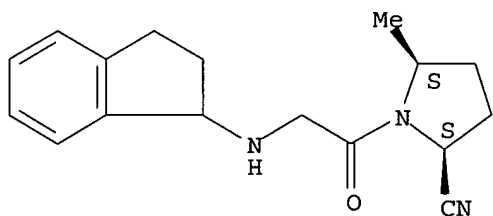
Absolute stereochemistry.



RN 676562-08-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(2,3-dihydro-1H-inden-1-yl)amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

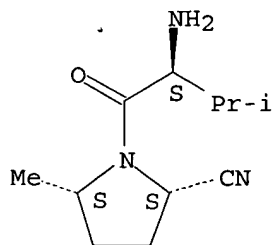
Absolute stereochemistry.



RN 676562-09-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3-methyl-1-oxobutyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

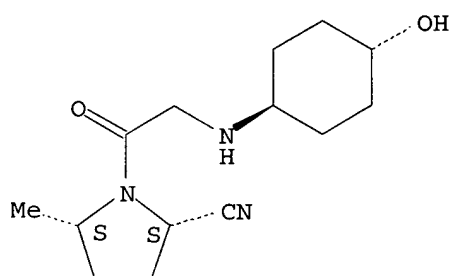
Absolute stereochemistry.



RN 676562-10-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(trans-4-hydroxycyclohexyl)amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

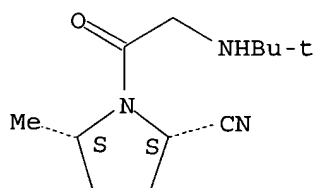
Absolute stereochemistry.



RN 676562-11-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(1,1-dimethylethyl)amino]acetyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

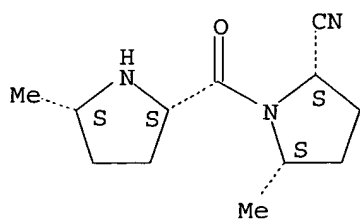
Absolute stereochemistry.



RN 676562-12-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-methyl-1-[[[(2S,5S)-5-methyl-2-pyrrolidinyl]carbonyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

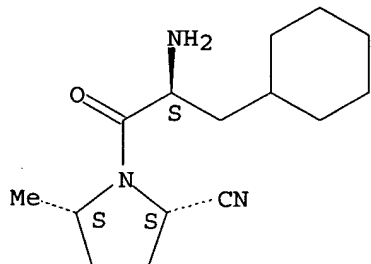
Absolute stereochemistry.



RN 676562-13-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3-cyclohexyl-1-oxopropyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

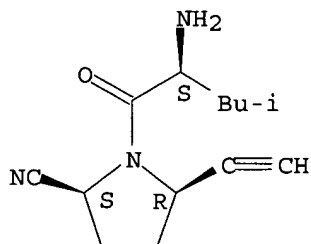
Absolute stereochemistry.



RN 676562-14-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

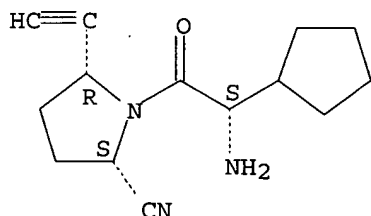
Absolute stereochemistry.



RN 676562-15-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclopentylacetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

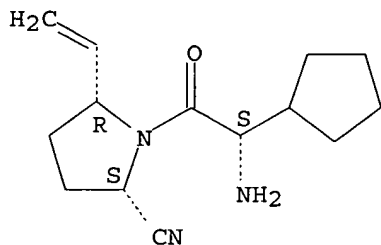
Absolute stereochemistry.



RN 676562-16-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclopentylacetyl]-5-ethenyl-, (2S,5R)- (9CI) (CA INDEX NAME)

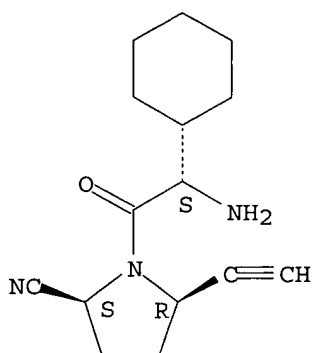
Absolute stereochemistry.



RN 676562-18-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-aminocyclohexylacetyl]-5-ethynyl-,
(2S,5R)-(9CI) (CA INDEX NAME)

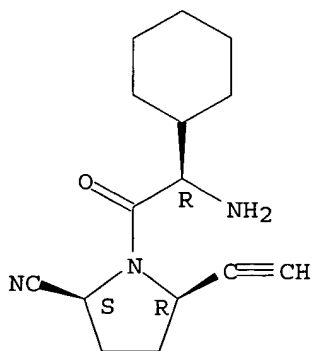
Absolute stereochemistry.



RN 676562-19-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2R)-aminocyclohexylacetyl]-5-ethynyl-,
(2S,5R)-(9CI) (CA INDEX NAME)

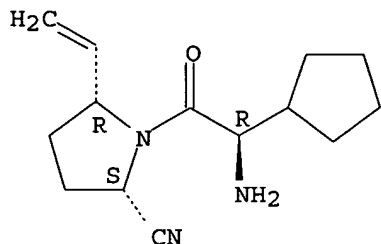
Absolute stereochemistry.



RN 676562-20-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2R)-aminocyclopentylacetyl]-5-ethynyl-,
(2S,5R)-(9CI) (CA INDEX NAME)

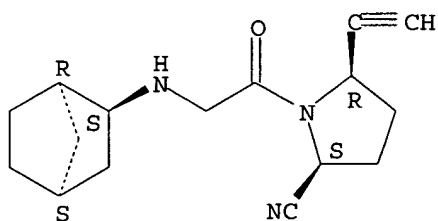
Absolute stereochemistry.



RN 676562-21-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(1R,2S,4S)-bicyclo[2.2.1]hept-2-ylamino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

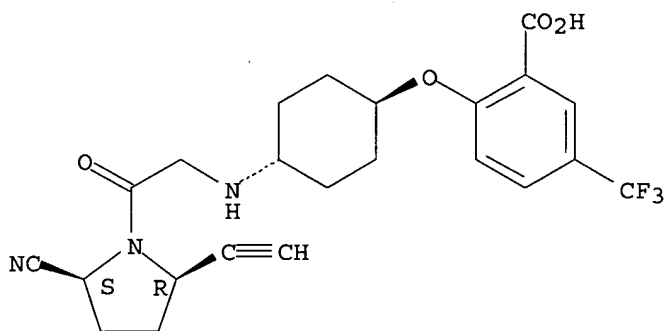
Absolute stereochemistry.



RN 676562-22-4 CAPLUS

CN Benzoic acid, 2-[[[trans-4-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]cyclohexyl]oxy]-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)

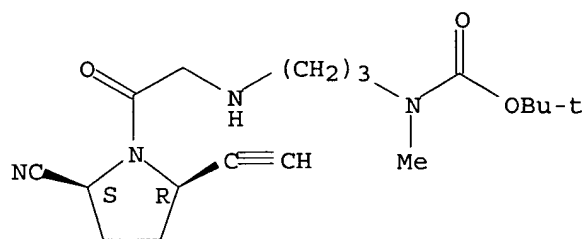
Absolute stereochemistry.



RN 676562-23-5 CAPLUS

CN Carbamic acid, [3-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]propyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

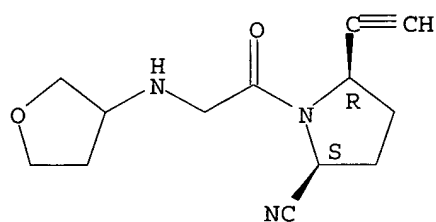
Absolute stereochemistry.



RN 676562-24-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[tetrahydro-3-furanyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

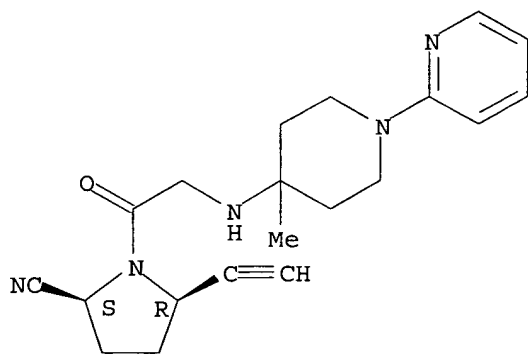
Absolute stereochemistry.



RN 676562-25-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-(2-pyridinyl)-4-piperidinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

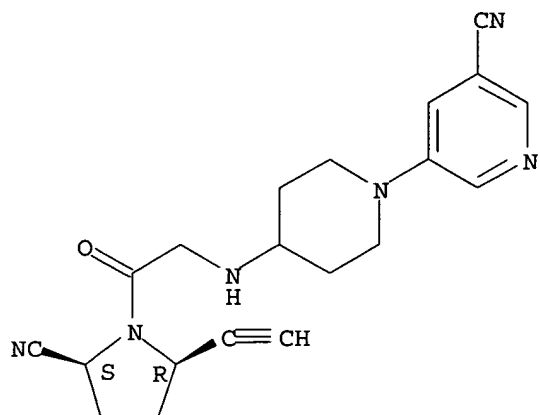
Absolute stereochemistry.



RN 676562-26-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-3-pyridinyl)-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

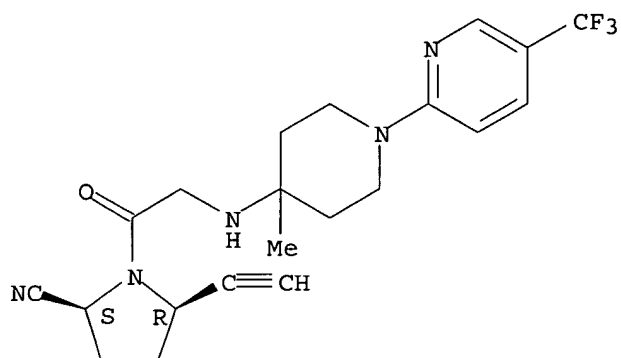
Absolute stereochemistry.



RN 676562-27-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[5-(trifluoromethyl)-2-pyridinyl]-4-piperidinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

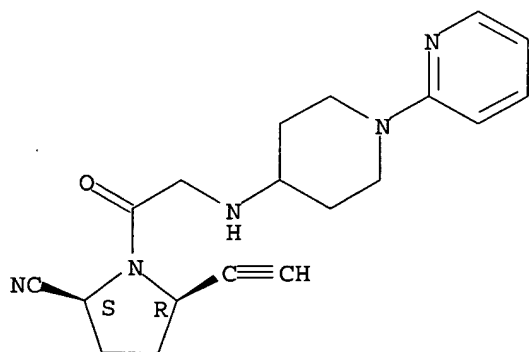
Absolute stereochemistry.



RN 676562-28-0 CAPLUS

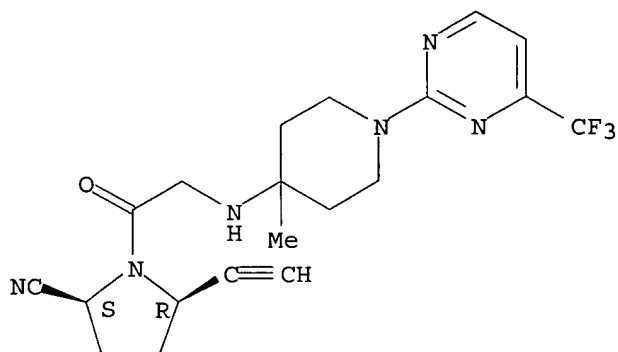
CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1-(2-pyridinyl)-4-piperidinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



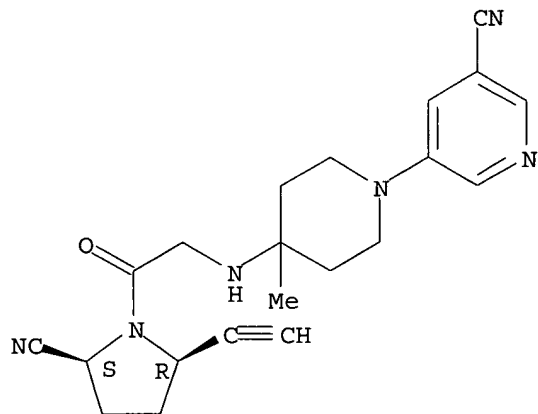
RN 676562-29-1 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-methyl-1-[4-(trifluoromethyl)-2-pyrimidinyl]-4-piperidinyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



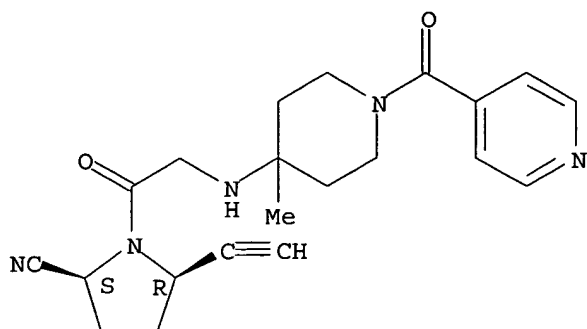
RN 676562-30-4 CAPLUS
 CN 2-Pyrrolidinecarbonitrile, 1-[[[1-(5-cyano-3-pyridinyl)-4-methyl-4-piperidinyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676562-31-5 CAPLUS
 CN 4-Piperidinamine, N-[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]-4-methyl-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

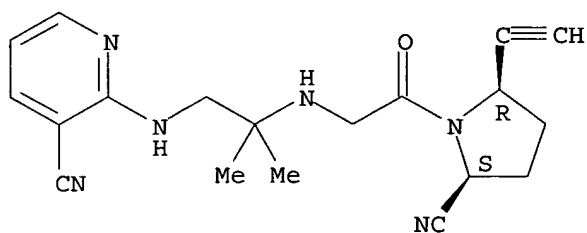
Absolute stereochemistry.



RN 676562-32-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(3-cyano-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-5-ethynyl-, (2S,5R)- (9CI) (CA INDEX NAME)

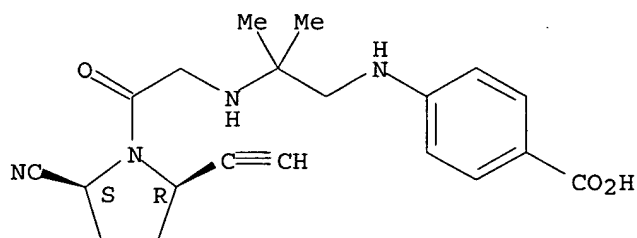
Absolute stereochemistry.



RN 676562-33-7 CAPLUS

CN Benzoic acid, 4-[[[2-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-2-methylpropyl]amino]- (9CI) (CA INDEX NAME)

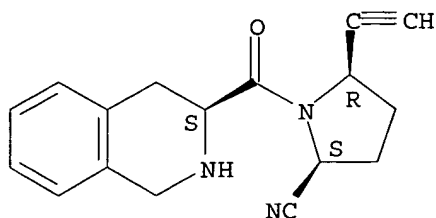
Absolute stereochemistry.



RN 676562-34-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[(3S)-1,2,3,4-tetrahydro-3-isoquinolinyl]carbonyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

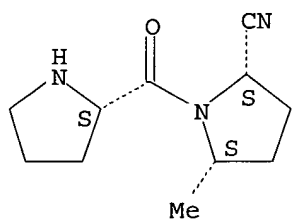
Absolute stereochemistry.



RN 676562-35-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-methyl-1-[(2S)-2-pyrrolidinylcarbonyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

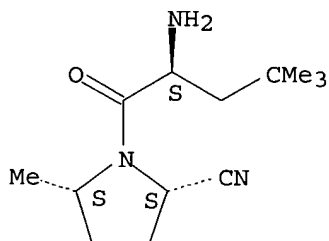
Absolute stereochemistry.



RN 676565-48-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-4,4-dimethyl-1-oxopentyl]-5-methyl-, (2S,5S)- (9CI) (CA INDEX NAME)

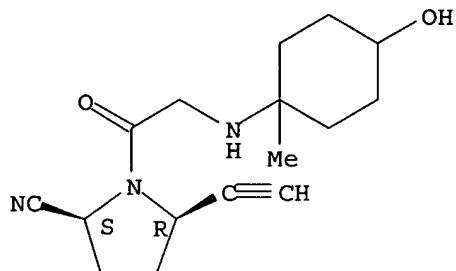
Absolute stereochemistry.



RN 676597-84-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[4-hydroxy-1-methylcyclohexyl)amino]acetyl]-, monohydrochloride, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

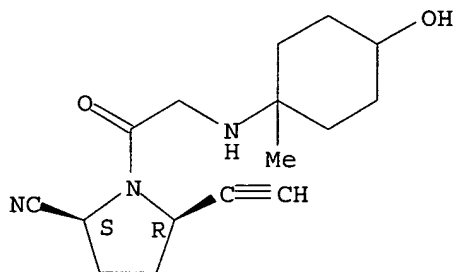


● HCl

RN 676597-85-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-hydroxy-1-methylcyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

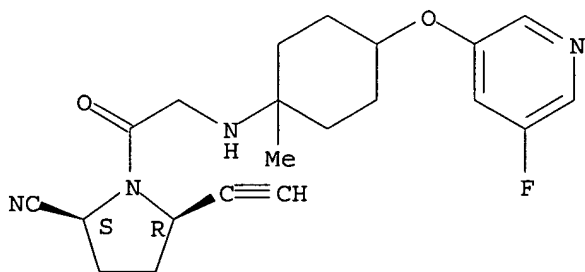
Absolute stereochemistry.



RN 676597-86-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-[(5-fluoro-3-pyridinyl)oxy]-1-methylcyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

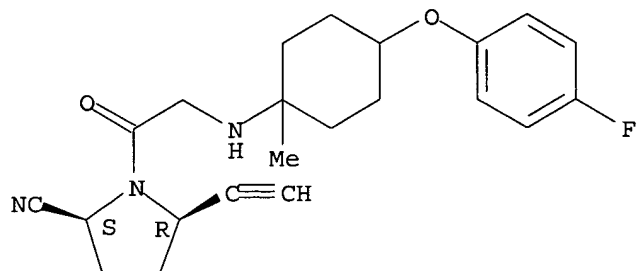
Absolute stereochemistry.



RN 676597-87-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-(4-fluorophenoxy)-1-methylcyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

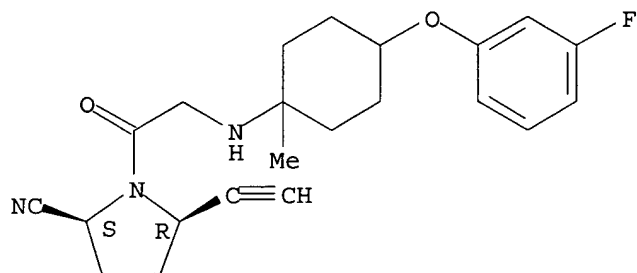
Absolute stereochemistry.



RN 676597-88-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[4-(3-fluorophenoxy)-1-methylcyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

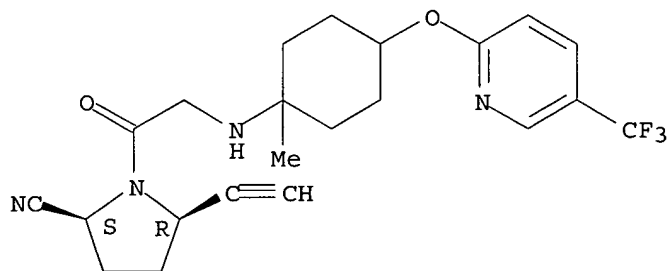
Absolute stereochemistry.



RN 676597-89-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 5-ethynyl-1-[[[1-methyl-4-[[5-(trifluoromethyl)-2-pyridinyl]oxy]cyclohexyl]amino]acetyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 676559-45-8P 676559-46-9P 676559-52-7P
 676559-53-8P 676559-55-0P 676559-60-7P
 676559-62-9P 676560-88-6P 676560-89-7P
 676560-95-5P 676560-96-6P 676561-18-5P
 676561-19-6P 676561-23-2P 676561-24-3P
 676561-25-4P 676561-77-6P

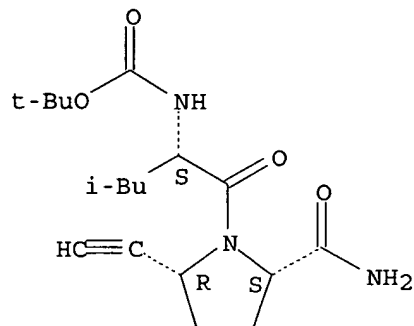
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of N-aminoacyl pyrrolidine-2-carbonitriles and related compds. as inhibitors of dipeptidyl peptidase-IV useful against type II diabetes and other disorders)

RN 676559-45-8 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl-5-ethynyl-, (5R)-(9CI) (CA INDEX NAME)

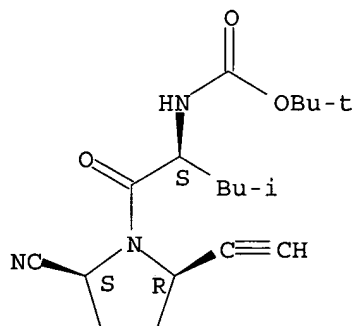
Absolute stereochemistry.



RN 676559-46-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

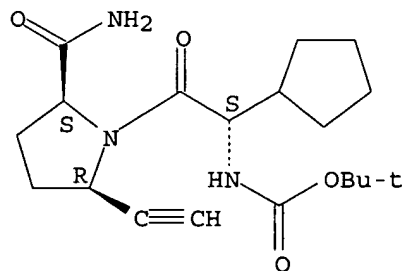
Absolute stereochemistry.



RN 676559-52-7 CAPLUS

CN L-Prolinamide, (2S)-2-cyclopentyl-N-[(1,1-dimethylethoxy)carbonyl]glycyl-5-ethynyl-, (5R)-(9CI) (CA INDEX NAME)

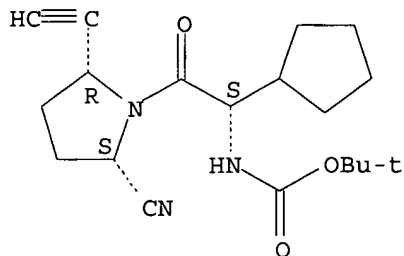
Absolute stereochemistry.



RN 676559-53-8 CAPLUS

CN Carbamic acid, [(1S)-2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-1-cyclopentyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

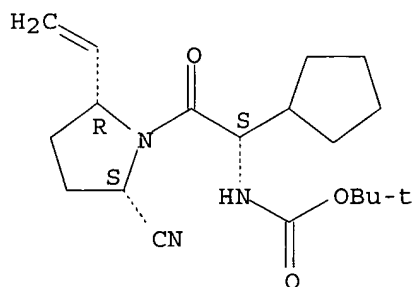
Absolute stereochemistry.



RN 676559-55-0 CAPLUS

CN Carbamic acid, [(1S)-2-[(2S,5R)-2-cyano-5-ethenyl-1-pyrrolidinyl]-1-cyclopentyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

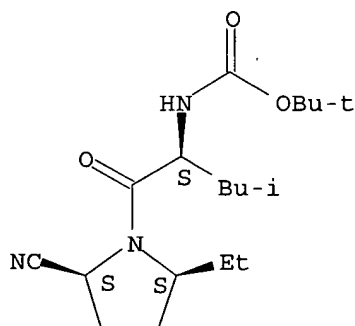
Absolute stereochemistry.



RN 676559-60-7 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(2S,5S)-2-cyano-5-ethyl-1-pyrrolidinyl]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

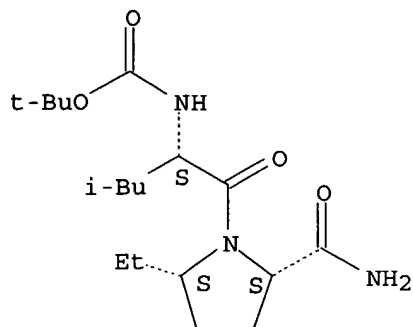
Absolute stereochemistry.



RN 676559-62-9 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl-5-ethyl-, (5S)- (9CI) (CA INDEX NAME)

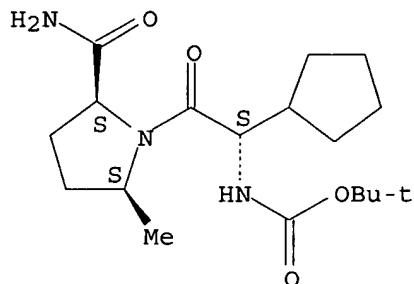
Absolute stereochemistry.



RN 676560-88-6 CAPLUS

CN Carbamic acid, [(1S)-2-[(2S,5S)-2-(aminocarbonyl)-5-methyl-1-pyrrolidinyl]-1-cyclopentyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

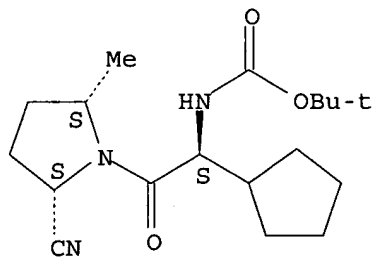
Absolute stereochemistry.



RN 676560-89-7 CAPLUS

CN Carbamic acid, [(1S)-2-[(2S,5S)-2-cyano-5-methyl-1-pyrrolidinyl]-1-cyclopentyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

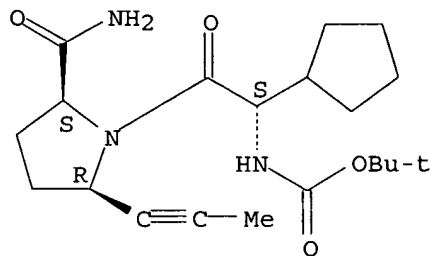
Absolute stereochemistry.



RN 676560-95-5 CAPLUS

CN L-Prolinamide, (2S)-2-cyclopentyl-N-[(1,1-dimethylethoxy)carbonyl]glycyl-5-(1-propynyl)-, (5R)- (9CI) (CA INDEX NAME)

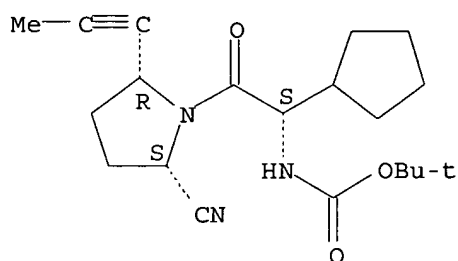
Absolute stereochemistry.



RN 676560-96-6 CAPLUS

CN Carbamic acid, [(1S)-2-[(2S,5R)-2-cyano-5-(1-propynyl)-1-pyrrolidinyl]-1-cyclopentyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

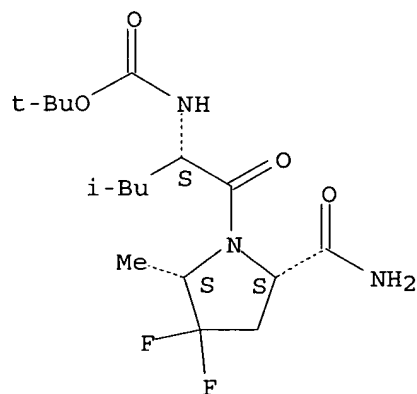
Absolute stereochemistry.



RN 676561-18-5 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl-4,4-difluoro-5-methyl-, (5S)- (9CI) (CA INDEX NAME)

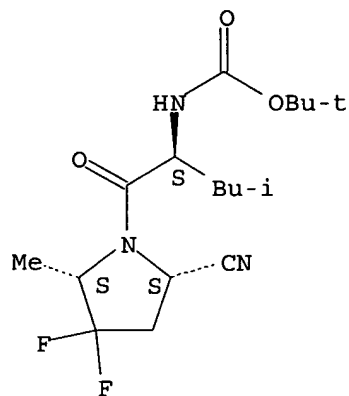
Absolute stereochemistry.



RN 676561-19-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(2S,5S)-5-cyano-3,3-difluoro-2-methyl-1-pyrrolidinyl]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

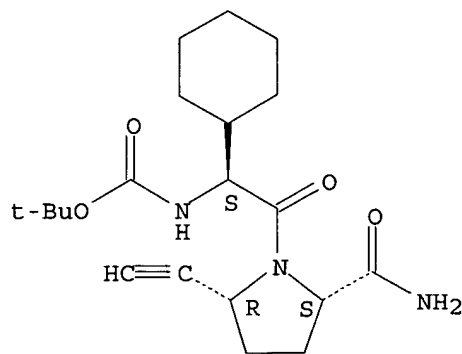
Absolute stereochemistry.



RN 676561-23-2 CAPLUS

CN L-Prolinamide, (2S)-2-cyclohexyl-N-[(1,1-dimethylethoxy)carbonyl]glycyl-5-ethynyl-, (5R)- (9CI) (CA INDEX NAME)

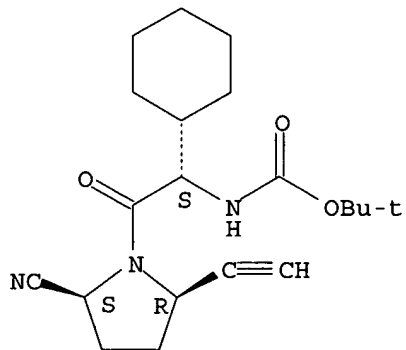
Absolute stereochemistry.



RN 676561-24-3 CAPLUS

CN Carbamic acid, [(1S)-2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-1-cyclohexyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

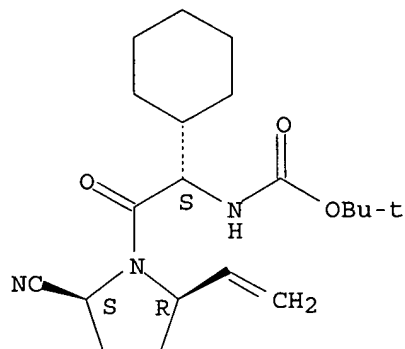
Absolute stereochemistry.



RN 676561-25-4 CAPLUS

CN Carbamic acid, [(1S)-2-[(2S,5R)-2-cyano-5-ethenyl-1-pyrrolidinyl]-1-cyclohexyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

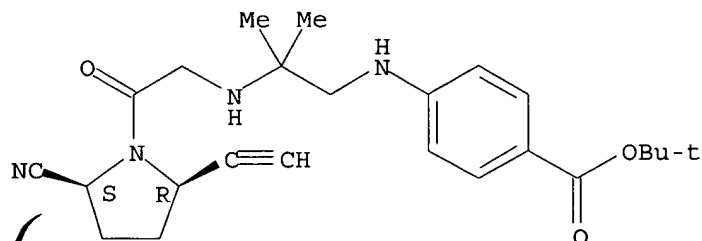
Absolute stereochemistry.



RN 676561-77-6 CAPLUS

CN Benzoic acid, 4-[[2-[[2-[(2S,5R)-2-cyano-5-ethynyl-1-pyrrolidinyl]-2-oxoethyl]amino]-2-methylpropyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



✓ L51 ANSWER 11 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:912843 CAPLUS

DOCUMENT NUMBER: 139:381756

TITLE: Preparation of peptides as NS3-serine protease inhibitors of hepatitis C virus

INVENTOR(S): Saksena, Anil K.; Girijavallabhan, Viyyoor Moopil; Lovey, Raymond G.; Jao, Edwin; Bennett, Frank; McCormick, Jinping L.; Wang, Haiyan; Pike, Russell E.; Bogen, Stephane L.; Chan, Tin-Yau; Liu, Yi-tsung; Zhu, Zhaoning; Njoroge, F. George; Arasappan, Ashok; Parekh, Tejal; Ganguly, Ashit K.; Chen, Kevin X.; Venkatraman, Srikanth; Vaccaro, Henry A.; Pinto, Patrick A.; Santhanam, Bama; Kemp, Scott Jeffrey; Levy, Odile Esther; Lim-Wilby, Marguerita; Tamura, Susan Y.; Wu, Wanli; Hendrata, Siska; Huang, Yuhua

PATENT ASSIGNEE(S): Schering Corporation, USA; Dendreon Corporation

SOURCE: U.S. Pat. Appl. Publ., 629 pp.

CODEN: USXXCO

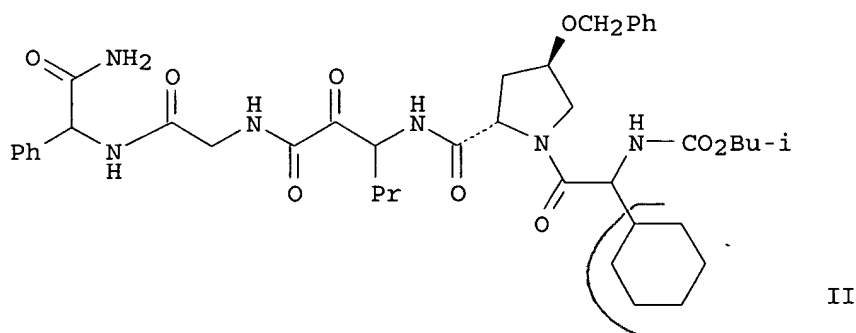
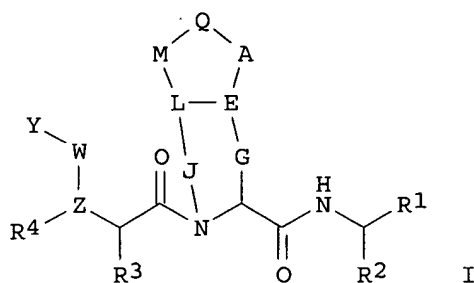
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|-------------------|----------|-----------------|------------|
| US 2003216325 | A1 | 20031120 | US 2001-908955 | 20010719 |
| US 2004254117 | A9 | 20041216 | | |
| US <u>7012066</u> | B2 | 20060314 | | |
| CN 1498224 | A | 20040519 | CN 2001-813111 | 20010719 |
| ZA 2002010312 | A | 20040329 | ZA 2002-10312 | 20021219 |
| PRIORITY APPLN. INFO.: | | | US 2000-220108P | P 20000721 |
| OTHER SOURCE(S): | MARPAT 139:381756 | | | |
| GI | | | | |



AB The invention discloses novel peptides I [Y is alkyl, alkylaryl, heteroalkyl, heteroaryl, aryl- or alkylheteroaryl, cycloalkyl, alkyloxy, alkylaryloxy, aryloxy, heteroaryloxy, heterocycloalkyloxy, cycloalkyloxy, alkylamino, arylamino, alkylarylamino, arylamino, heteroarylamino, cycloalkylamino, or heterocycloalkylamino; R1 is acyl; Z is O, N, CH or CR; R, R2-R4 are H, alkyl, alkenyl, cycloalkyl, heterocycloalkyl, alkoxy, aryloxy, alkylthio, arylthio, amino, amido, ester, carboxylic acid, carbamate, urea, ketone, aldehyde, cyano, nitro, halo, (cycloalkyl)alkyl, or (heterocycloalkyl)alkyl; W, Q, G, J, L, M independently may be present or absent; W is CO, CS, C(:N-CN), or SO₂; Q is CH, N, P, alkylidene, O, NR, S, or SO₂; A is O, CH, alkylidene, NR, S, SO₂, or a bond; E is CH, N, alkylidene, or a double bond; G is alkylidene; J is alkylidene, SO₂, NH, NR, or O; L is CH, CR, O, S, or NR; M is O, NR, S, SO₂, or alkylidene (with provisos)] which have HCV protease inhibitory activity as well as methods for preparing such compds. In another embodiment, the invention discloses pharmaceutical compns. comprising such compds. as well as

methods of using them to treat disorders associated with the HCV protease. Thus, peptide II was prepared by the solid-phase method and showed $K_i = 1-100$ nM (category A) in the HCV continuous assay.

IT 394723-48-9P 394723-49-0P 394723-56-9P
394723-61-6P 394723-62-7P 394728-85-9P
394730-92-8P 395661-13-9P

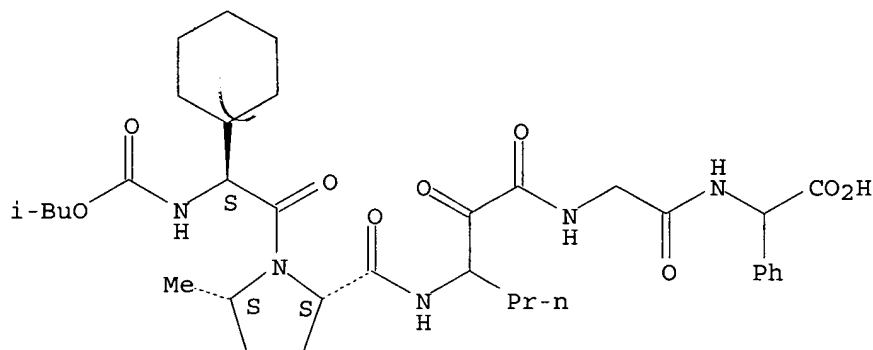
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptides as NS3-serine protease inhibitors of hepatitis C virus)

RN 394723-48-9 CAPLUS

CN Glycine, (2S)-2-cyclohexyl-N-[(2-methylpropoxy)carbonyl]glycyl-(5S)-5-methyl-L-prolyl-3-amino-2-oxohexanoylglycyl-2-phenyl- (9CI) (CA INDEX NAME)

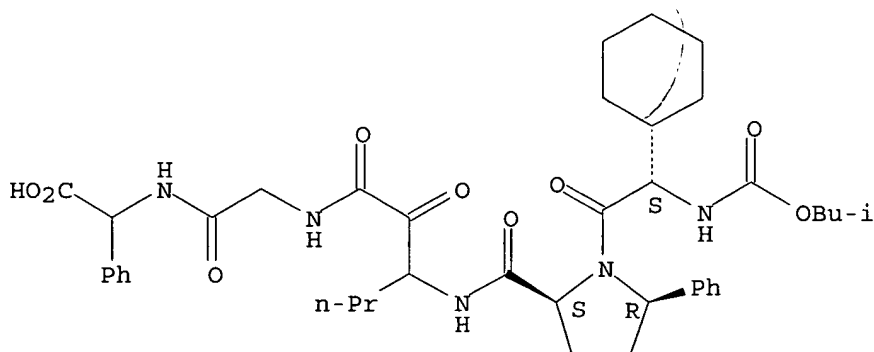
Absolute stereochemistry.



RN 394723-49-0 CAPLUS

CN Glycine, (2S)-2-cyclohexyl-N-[(2-methylpropoxy)carbonyl]glycyl-(5R)-5-phenyl-L-prolyl-3-amino-2-oxohexanoylglycyl-2-phenyl- (9CI) (CA INDEX NAME)

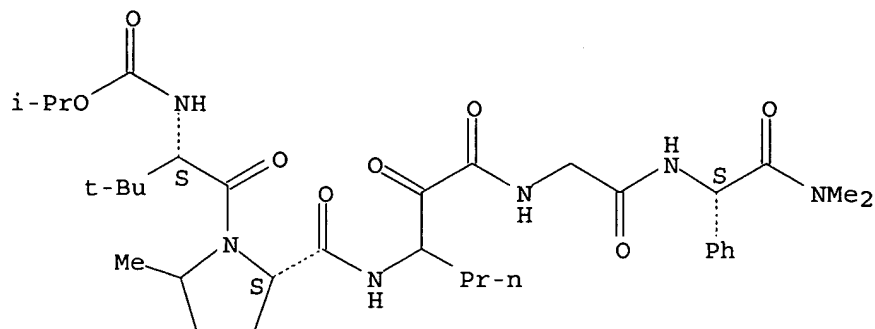
Absolute stereochemistry.



RN 394723-56-9 CAPLUS

CN Glycinamide, 3-methyl-N-[(1-methylethoxy)carbonyl]-L-valyl-4-methyl-L-prolyl-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)- (9CI) (CA INDEX NAME)

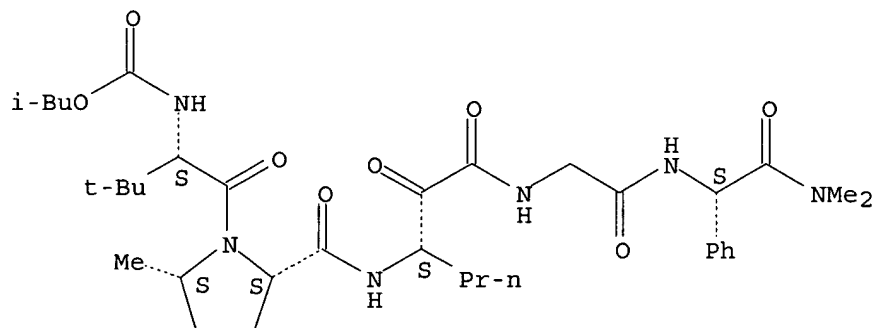
Absolute stereochemistry.



RN 394723-61-6 CAPLUS

CN Glycinamide, 3-methyl-N-[(2-methylpropoxy)carbonyl]-L-valyl-(5S)-5-methyl-L-prolyl-(3S)-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)-(9CI) (CA INDEX NAME)

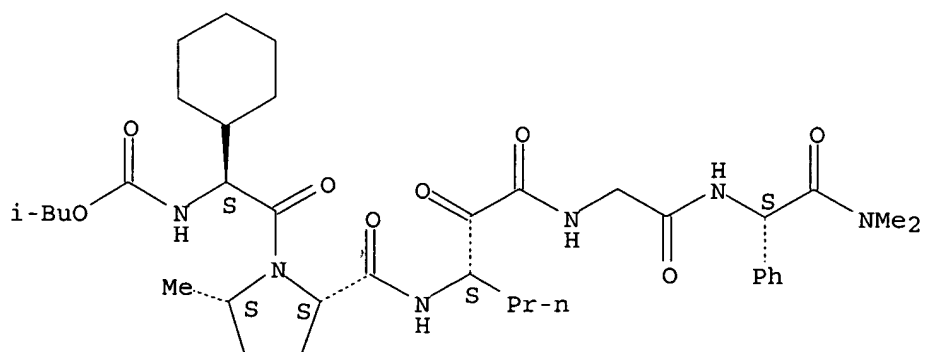
Absolute stereochemistry.



RN 394723-62-7 CAPLUS

CN Glycinamide, (2S)-2-cyclohexyl-N-[(2-methylpropoxy)carbonyl]glycyl-(5S)-5-methyl-L-prolyl-(3S)-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)-(9CI) (CA INDEX NAME)

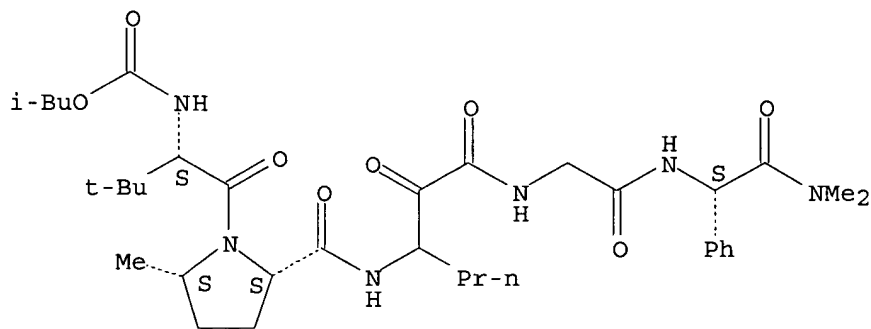
Absolute stereochemistry.



RN 394728-85-9 CAPLUS

CN Glycinamide, 3-methyl-N-[(2-methylpropoxy)carbonyl]-L-valyl-(5S)-5-methyl-L-prolyl-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)- (9CI)
(CA INDEX NAME)

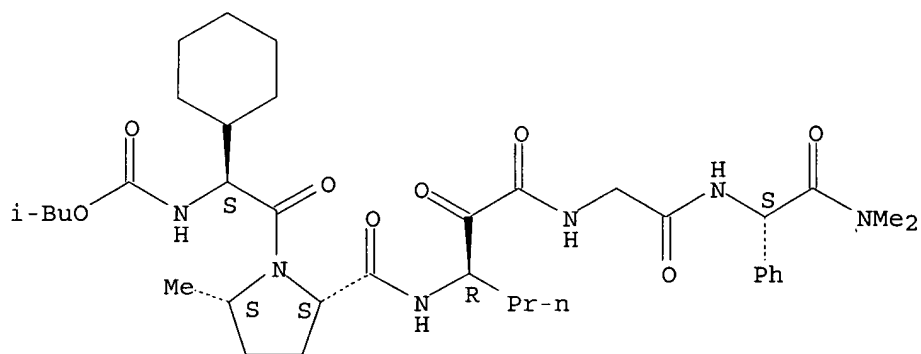
Absolute stereochemistry.



RN 394730-92-8 CAPLUS

CN Glycinamide, (2S)-2-cyclohexyl-N-[(2-methylpropoxy)carbonyl]glycyl-(5S)-5-methyl-L-prolyl-(3R)-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)- (9CI) (CA INDEX NAME)

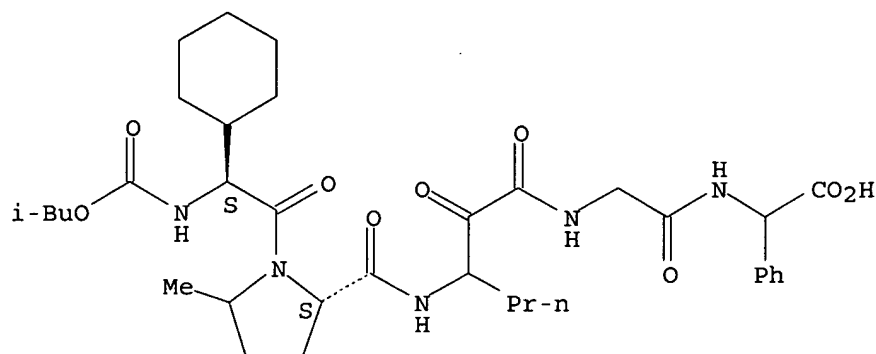
Absolute stereochemistry.



RN 395661-13-9 CAPLUS

CN Glycine, (2S)-2-cyclohexyl-N-[(2-methylpropoxy)carbonyl]glycyl-5-methyl-L-prolyl-3-amino-2-oxohexanoylglycyl-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 111 THERE ARE 111 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 12 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:591204 CAPLUS

DOCUMENT NUMBER: 139:149928

TITLE: Preparation of peptides as NS3-serine protease inhibitors of hepatitis C virus

INVENTOR(S): Saksena, Anil K.; Girijavallabh, Viyyoor M.; Lovey, Raymond G.; Jao, Edwin; Bennett, Frank; McCormick, Jinping L.; Wang, Haiyan; Pike, Russell E.; Bogen, Stephane L.; Chan, Tin-yau; Liu, Yi-tsung; Zhu, Zhaoning; Njoroge, George F.; Arasappan, Ashok; Parekh, Tejal; Ganguly, Ashit K.; Chen, Kevin X.; Venkatraman, Srikanth; Vaccaro, Henry A.; Pinto, Patrick A.; Santhanam, Bama; Kemp, Scott Jeffrey; Levy, Odile Esther; Lim-Wilby, Marguerita; Tamura, Susan Y.; Wu, Wanli; Hendrata, Siska; Huang, Yuhua; Wong, Jesse K.; Nair, Latha G.

PATENT ASSIGNEE(S): Schering Corporation, USA; Corvas International, Inc.; Dendreon Corp.

SOURCE: PCT Int. Appl., 633 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2003062265 | A2 | 20030731 | WO 2003-US1430 | 20030116 |
| WO 2003062265 | A3 | 20040916 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM | | | |
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| CA 2473032 | AA | 20030731 | CA 2003-2473032 | 20030116 |
| EP 1481000 | A2 | 20041201 | EP 2003-731956 | 20030116 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

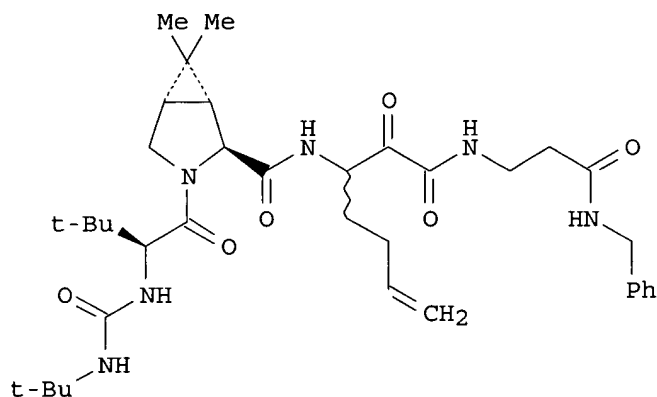
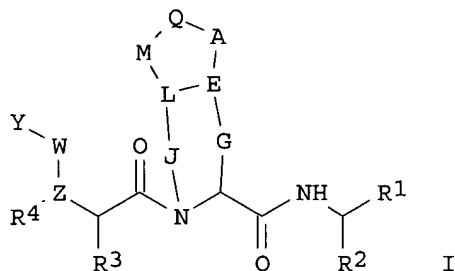
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| BR 2003006931 | A | 20050419 | BR 2003-6931 | 20030116 |
| CN 1633446 | A | 20050629 | CN 2003-805933 | 20030116 |
| JP 2005524628 | T2 | 20050818 | JP 2003-562142 | 20030116 |
| NO 2004002792 | A | 20041015 | NO 2004-2792 | 20040702 |

PRIORITY APPLN. INFO.:

| | | |
|----------------|---|----------|
| US 2002-52386 | A | 20020118 |
| WO 2003-US1430 | W | 20030116 |

OTHER SOURCE(S): MARPAT 139:149928

GI



II

AB The invention discloses novel peptides I [Y is alkyl, alkylaryl, heteroalkyl, heteroaryl, aryl- or alkylheteroaryl, cycloalkyl, alkyloxy, alkylaryloxy, aryloxy, heteroaryloxy, heterocycloalkyloxy, cycloalkyloxy, alkylamino, arylamino, alkylaryl amino, arylamino, heteroaryl amino, cycloalkyl amino, or heterocycloalkyl amino; R1 is acyl; Z is selected from O, N, CH or CR; R, R2-R4 are H, alkyl, alkenyl, cycloalkyl, heterocycloalkyl, alkoxy, aryloxy, alkylthio, arylthio, amino, amido, ester, carboxylic acid, carbamate, urea, ketone, aldehyde, cyano, nitro, halo, (cycloalkyl)alkyl, or (heterocycloalkyl)alkyl; W, Q, G, J, L, M independently may be present or absent; W is CO, CS, C(:N-CN), or SO2; Q is CH, N, P, alkylidene, O, NR, S, or SO2; A is O, CH, alkylidene, NR, S, SO2, or a bond; E is CH, N, alkylidene, or a double bond; G is alkylidene; J is alkylidene, SO2, NH, NR, or O; L is CH, CR, O, S, or NR; M is O, NR, S, SO2, or alkylidene (with provisos)] which have HCV protease inhibitory activity as well as methods for preparing such compds. In another embodiment, the invention discloses pharmaceutical compns. comprising such compds. as well as methods of using them to treat disorders associated with the HCV protease. Thus, peptide II was prepared and showed $K_i = 1-100$ nM (category A) in the HCV continuous assay.

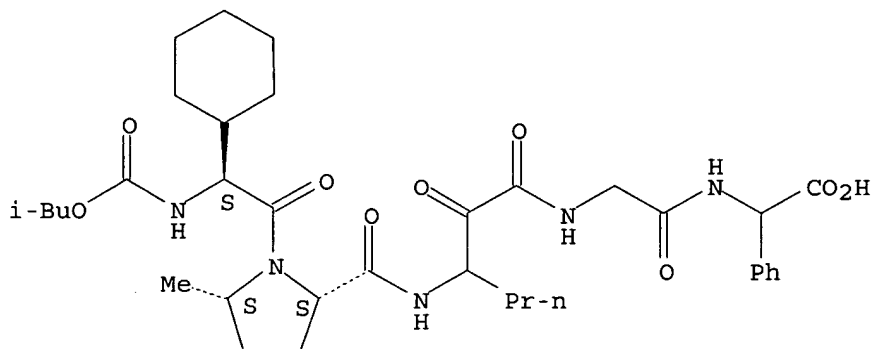
IT 394723-48-9P 394723-49-0P 394723-56-9P
 394723-61-6P 394723-62-7P 394727-43-6P
 394727-44-7P

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of peptides as NS3-serine protease inhibitors of hepatitis C virus)

RN 394723-48-9 CAPLUS

CN Glycine, (2S)-2-cyclohexyl-N-[(2-methylpropoxy)carbonyl]glycyl-(5S)-5-methyl-L-prolyl-3-amino-2-oxohexanoylglycyl-2-phenyl- (9CI) (CA INDEX NAME)

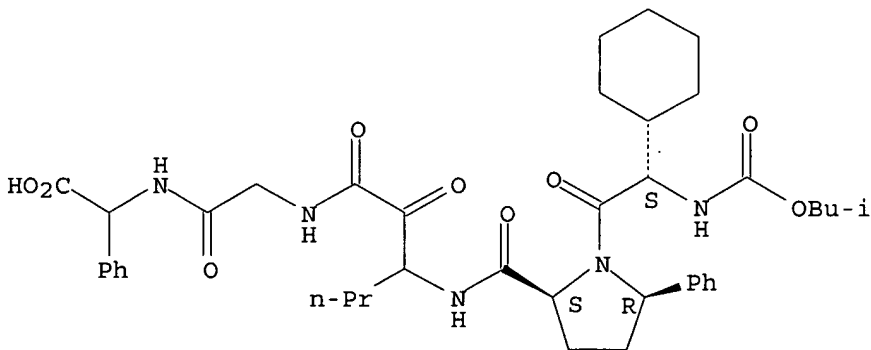
Absolute stereochemistry.



RN 394723-49-0 CAPLUS

CN Glycine, (2S)-2-cyclohexyl-N-[(2-methylpropoxy)carbonyl]glycyl-(5R)-5-phenyl-L-prolyl-3-amino-2-oxohexanoylglycyl-2-phenyl- (9CI) (CA INDEX NAME)

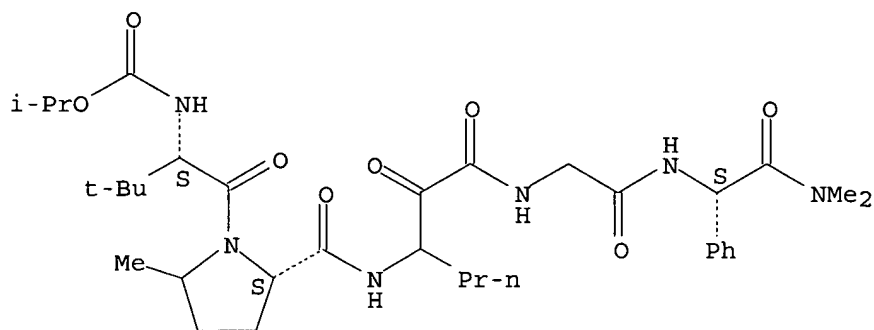
Absolute stereochemistry.



RN 394723-56-9 CAPLUS

CN Glycinamide, 3-methyl-N-[(1-methylethoxy)carbonyl]-L-valyl-4-methyl-L-prolyl-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)- (9CI) (CA INDEX NAME)

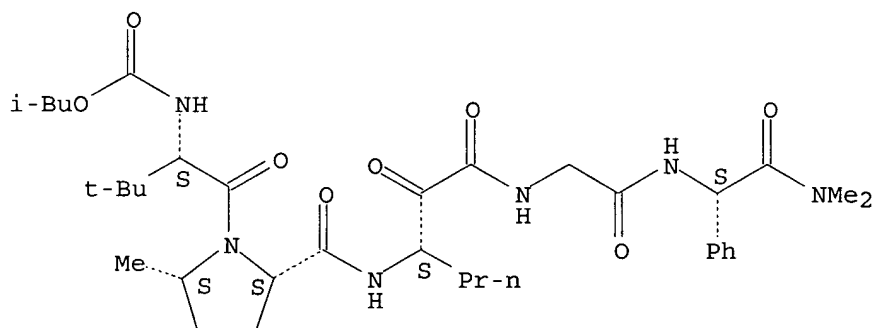
Absolute stereochemistry.



RN 394723-61-6 CAPLUS

CN Glycinamide, 3-methyl-N-[(2-methylpropoxy)carbonyl]-L-valyl-(5S)-5-methyl-L-prolyl-(3S)-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)-(9CI) (CA INDEX NAME)

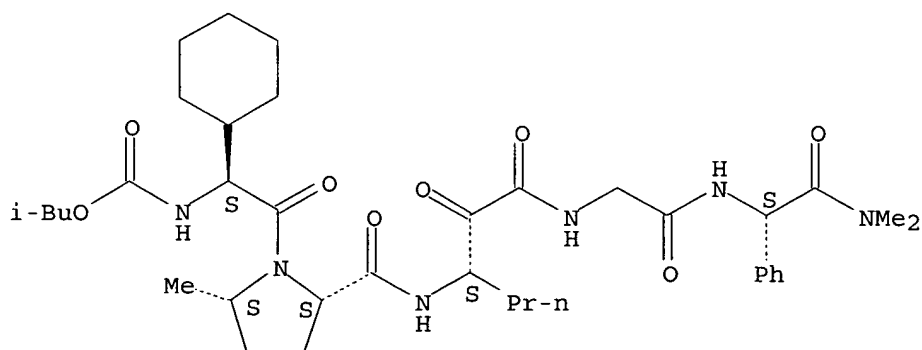
Absolute stereochemistry.



RN 394723-62-7 CAPLUS

CN Glycinamide, (2S)-2-cyclohexyl-N-[(2-methylpropoxy)carbonyl]glycyl-(5S)-5-methyl-L-prolyl-(3S)-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

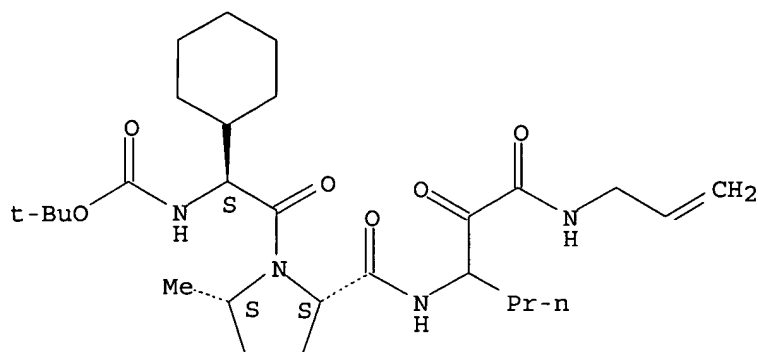


RN 394727-43-6 CAPLUS

CN L-Prolinamide, (2S)-2-cyclohexyl-N-[(1,1-dimethylethoxy)carbonyl]glycyl-5-

methyl-N-[1-[oxo(2-propenylamino)acetyl]butyl]-, (5S)- (9CI) (CA INDEX NAME)

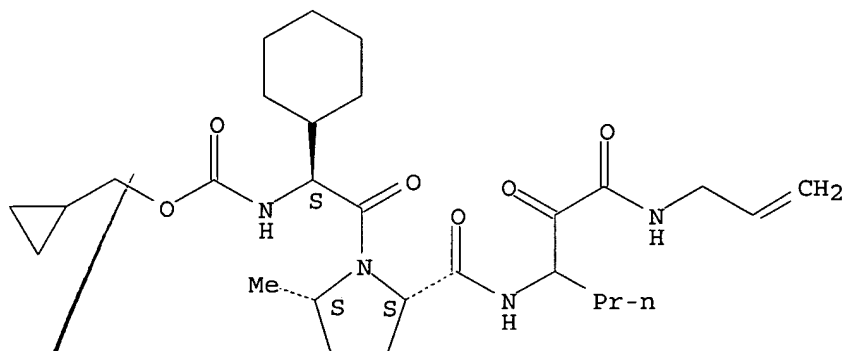
Absolute stereochemistry.



RN 394727-44-7 CAPLUS

CN L-Prolinamide, (2S)-2-cyclohexyl-N-[(cyclopropylmethoxy)carbonyl]glycyl-5-methyl-N-[1-[oxo(2-propenylamino)acetyl]butyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 13 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:509763 CAPLUS

DOCUMENT NUMBER: 140:218054

TITLE: Stabilization of type VIa β -turn in tetrapeptides

AUTHOR(S): Halab, Liliane; Lubell, William D.

CORPORATE SOURCE: Departement de chimie, Universite de Montreal, Montreal, QC, H3C 3J7, Can.

SOURCE: Peptides 2000, Proceedings of the European Peptide Symposium, 26th, Montpellier, France, Sept. 10-15, 2000 (2001), Meeting Date 2000, 815-816. Editor(s): Martinez, Jean; Fehrentz, Jean-Alain. Editions EDK: Paris, Fr.

CODEN: 69EDWK; ISBN: 2-84254-048-4

DOCUMENT TYPE: Conference

LANGUAGE: English

AB A symposium report. The factors stabilizing type VIa β -turns in

peptides were investigated by incorporating 5-tBuPro into a series of tetrapeptides possessing the general structure Ac-Ala-Xaa-5-tBuPro-Yaa-ZMe. The importance of the nature of the amino acids on either side of the 5-tBuPro residue was investigated.

IT 412303-28-7P 412303-29-8P 412303-30-1P

412303-31-2P 412303-32-3P 412303-33-4P

412303-34-5P 412303-36-7P 412303-38-9P

412303-41-4P

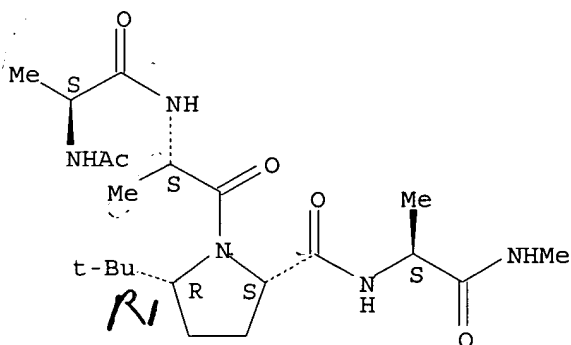
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)

(solution and solid phase synthesis of tetrapeptides containing 5-tBuPro and effect of nature of amino acids on β -turn stabilization by NMR)

RN 412303-28-7 CAPLUS

CN L-Alaninamide, N-acetyl-L-alanyl-L-alanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-N-methyl- (9CI) (CA INDEX NAME)

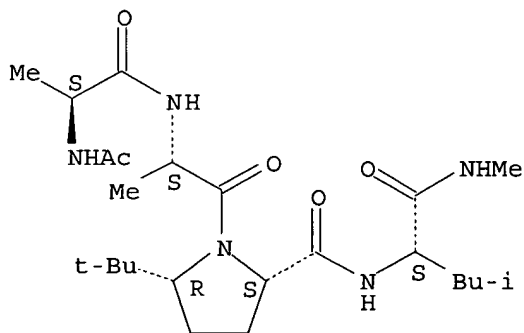
Absolute stereochemistry.



RN 412303-29-8 CAPLUS

CN L-Leucinamide, N-acetyl-L-alanyl-L-alanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-N-methyl- (9CI) (CA INDEX NAME)

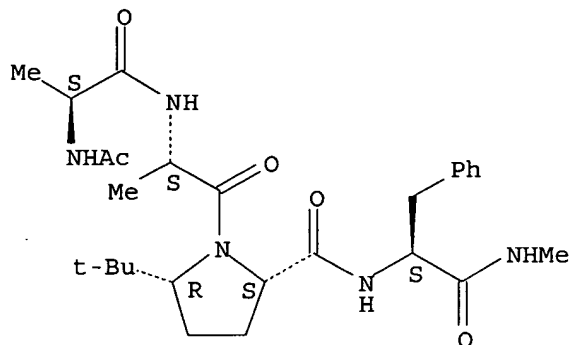
Absolute stereochemistry.



RN 412303-30-1 CAPLUS

CN L-Phenylalaninamide, N-acetyl-L-alanyl-L-alanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-N-methyl- (9CI) (CA INDEX NAME)

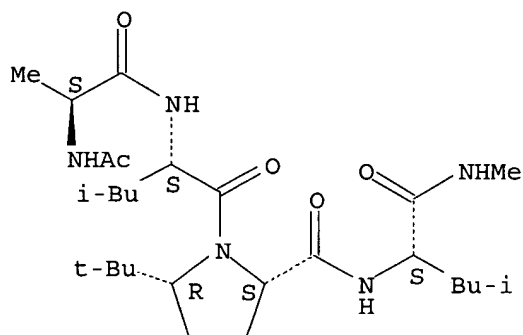
Absolute stereochemistry.



RN 412303-31-2 CAPLUS

CN L-Leucinamide, N-acetyl-L-alanyl-L-leucyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-N-methyl- (9CI) (CA INDEX NAME)

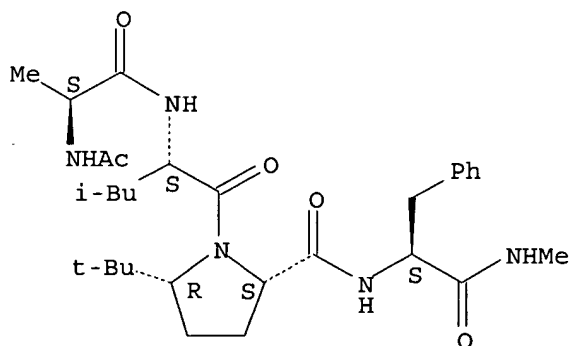
Absolute stereochemistry.



RN 412303-32-3 CAPLUS

CN L-Phenylalaninamide, N-acetyl-L-alanyl-L-leucyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-N-methyl- (9CI) (CA INDEX NAME)

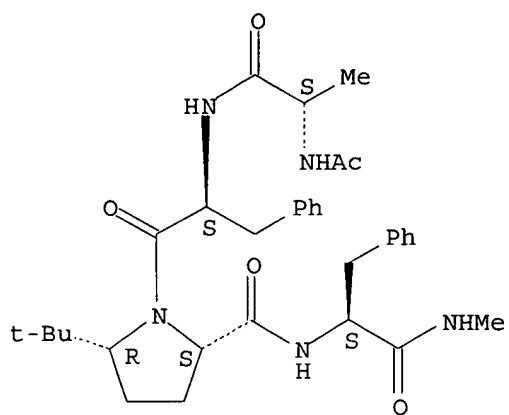
Absolute stereochemistry.



RN 412303-33-4 CAPLUS

CN L-Phenylalaninamide, N-acetyl-L-alanyl-L-phenylalanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-N-methyl- (9CI) (CA INDEX NAME)

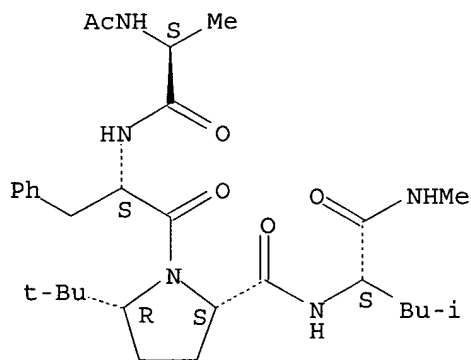
Absolute stereochemistry.



RN 412303-34-5 CAPLUS

CN L-Leucinamide, N-acetyl-L-alanyl-L-phenylalanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-N-methyl- (9CI) (CA INDEX NAME)

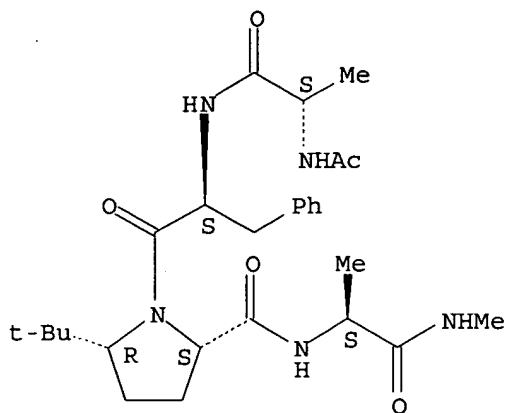
Absolute stereochemistry.



RN 412303-36-7 CAPLUS

CN L-Alaninamide, N-acetyl-L-alanyl-L-phenylalanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-N-methyl- (9CI) (CA INDEX NAME)

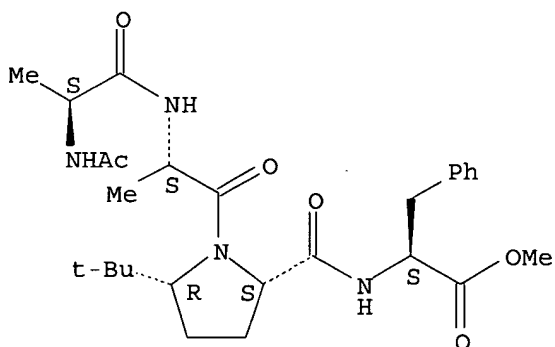
Absolute stereochemistry.



RN 412303-38-9 CAPLUS

CN L-Phenylalanine, N-acetyl-L-alanyl-L-alanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-, methyl ester (9CI) (CA INDEX NAME)

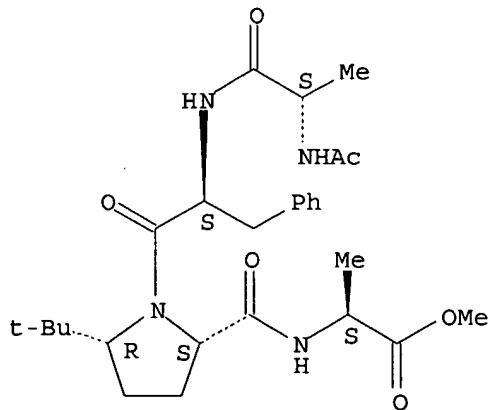
Absolute stereochemistry.



RN 412303-41-4 CAPLUS

CN L-Alanine, N-acetyl-L-alanyl-L-phenylalanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 14 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:509650 CAPLUS

DOCUMENT NUMBER: 140:87818

TITLE: Steric interactions of penicillamine6-5-tert-butylproline7-oxytocin analogs and their influence on conformation and biological activity

AUTHOR(S): Belec, Laurent; Slaninova, Jirina; Lubell, William D.

CORPORATE SOURCE: Departement de Chimie Universite de Montreal, Montreal, QC, H3C 3J7, Can.

SOURCE: Peptides 2000, Proceedings of the European Peptide Symposium, 26th, Montpellier, France, Sept. 10-15, 2000 (2001), Meeting Date 2000, 587-588. Editor(s): Martinez, Jean; Fehrentz, Jean-Alain. Editions EDK: Paris, Fr.

CODEN: 69EDWK; ISBN: 2-84254-048-4

DOCUMENT TYPE: Conference

LANGUAGE: English

AB Introduction of (2S,5R)-5-tert-butylproline (5-tBuPro) into a series of oxytocin (OT) analogs caused an augmentation of the prolyl amide cis-isomer population by steric interactions that destabilized the trans-conformer. Biol. evaluation of these analogs indicated a strong reduction in agonistic activity and a slight enhancement of antagonist potency. This provided addnl. evidence to support the hypothesis that the prolyl amide cis-isomer may favor antagonism and that the trans-isomer is necessary for agonist activity. To further explore this hypothesis, a second series of [5-tBuPro7]OT analogs was synthesized possessing Pen instead of Cys at position 6.

IT 323192-85-4D, analogs 323192-86-5 387868-19-1D, analogs 387868-21-5 387868-23-7 644990-99-8

RL: PRP (Properties)

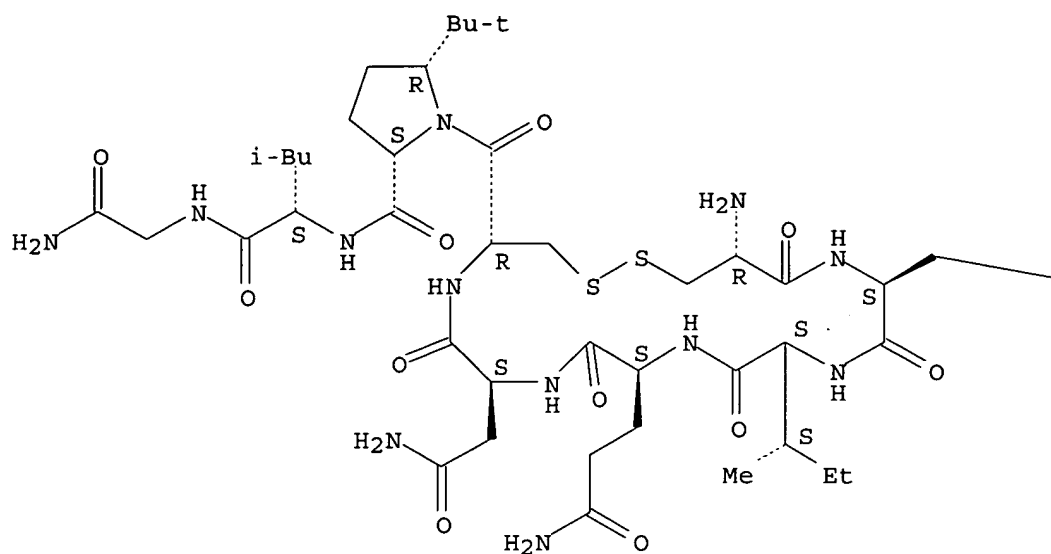
(steric interactions of penicillamine6-5-tert-butylproline7-oxytocin analogs and their influence on conformation and biol. activity)

RN 323192-85-4 CAPLUS

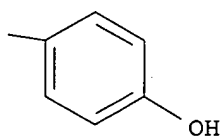
CN Oxytocin, 7-[(5R)-5-(1,1-dimethylethyl)-L-proline]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



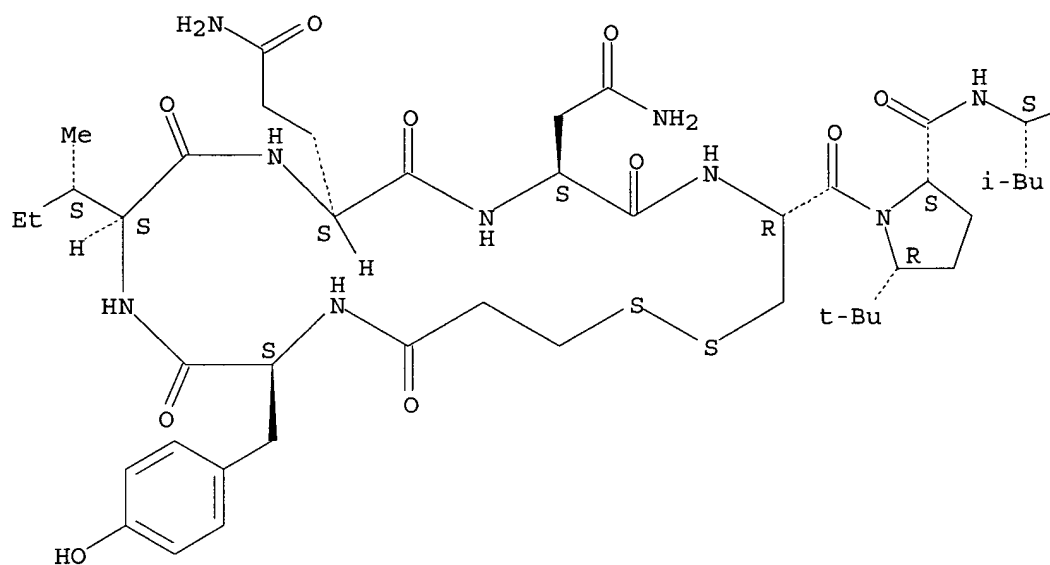
PAGE 1-B



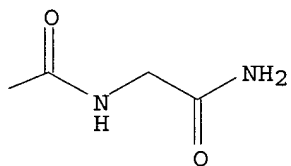
RN 323192-86-5 CAPLUS
 CN Glycinamide, N-(3-mercapto-1-oxopropyl)-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-L-leucyl-, cyclic (1-5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



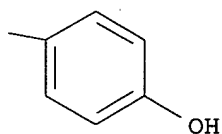
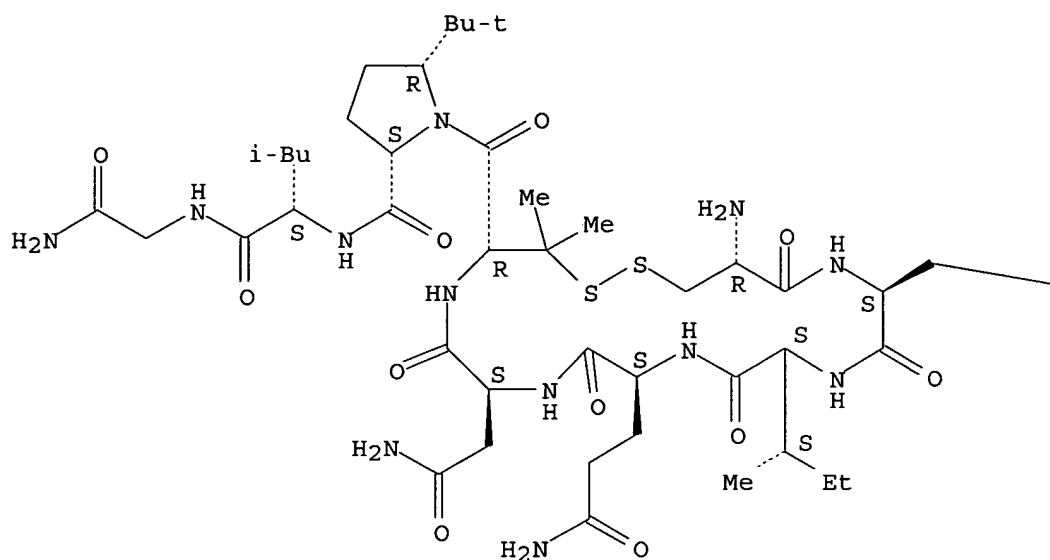
PAGE 1-B



RN 387868-19-1 CAPLUS

CN Glycinamide, L-cysteinyl-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-
 3-mercapto-L-valyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-L-leucyl-, cyclic
 (1→6)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

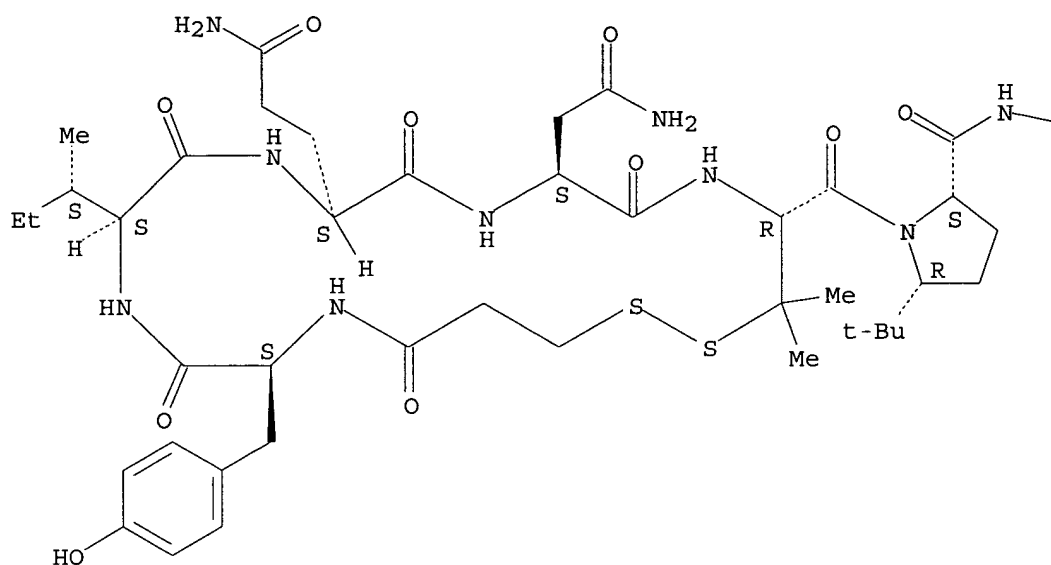


RN 387868-21-5 CAPLUS

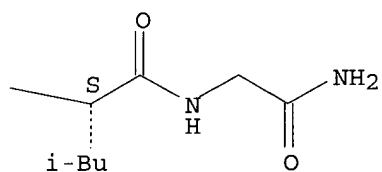
CN Glycinamide, N-(3-mercapto-1-oxopropyl)-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-3-mercapto-L-valyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-L-leucyl-, cyclic (1-5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

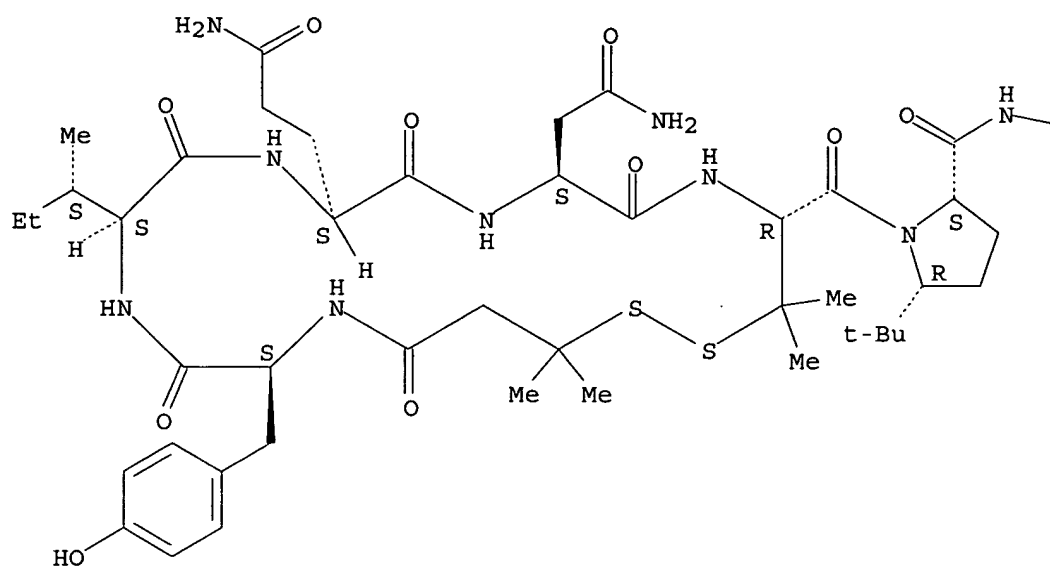


RN 387868-23-7 CAPLUS

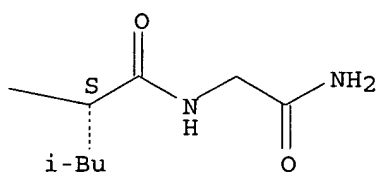
CN Glycinamide, N-(3-mercapto-3-methyl-1-oxobutyl)-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-3-mercapto-L-valyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-L-leucyl-, cyclic (1→5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

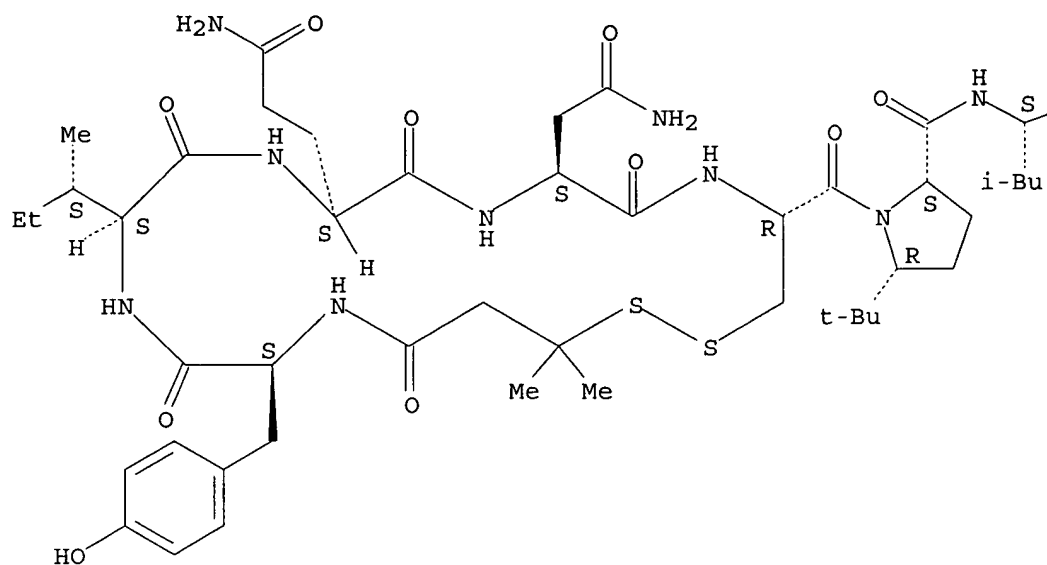


RN 644990-99-8 CAPLUS

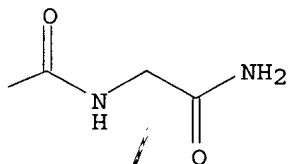
CN Glycinamide, N-(3-mercapto-3-methyl-1-oxobutyl)-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-L-leucyl-, cyclic (1-5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 15 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:928230 CAPLUS

DOCUMENT NUMBER: 138:19472

TITLE: Method of identifying inhibitors of Cdc25 using three dimensional crystal structure of the catalytic domain of Cdc25

INVENTOR(S): Taylor, Neil R.; Borhani, David; Epstein, David; Rudolph, Johannes; Ritter, Kurt; Fujimori, Taro; Robinson, Simon; Eckstein, Jens; Haupt, Andreas; Walker, Nigel; Dixon, Richard W.; Choquette, Deborah; Blanchard, Jill; Kluge, Arthur; Pal, Kollol; Bockovich, Nicholas; Come, Jon; Hediger, Mark

PATENT ASSIGNEE(S): Australia

SOURCE: U.S. Pat. Appl. Publ., 246 pp., Cont.-in-part of U.S. Ser. No. 645,750.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2002183249 | A1 | 20021205 | US 2001-797500 | 20010301 |
| PRIORITY APPLN. INFO.: | | | US 1999-172215P | P 19990831 |
| | | | US 2000-645750 | A2 20000824 |

OTHER SOURCE(S): MARPAT 138:19472

AB The present invention relates to the x-ray crystallog. study of proteins comprising the catalytic domains of Cdc25. The atomic coordinates which result from this study are of use in identifying compds. which fit in the catalytic domain and are, therefore, potential inhibitors of Cdc25. The present invention further provides proteins which comprise the ligand binding domain of Cdc25, crystalline forms of these proteins and the use of these crystalline forms to determine the three dimensional structure of the catalytic domain of Cdc25. The invention also relates to the use of the three dimensional structure of the Cdc25 catalytic domain in methods of designing and/or identifying potential inhibitors of Cdc25 activity, for example, compds. which inhibit the binding of a native substrate to the Cdc25 catalytic domain. These Cdc25 inhibitors are of use in methods of treating a patient having a condition which is modulated by Cdc25 activity, for example, a condition characterized by excessive, inappropriate or undesirable cellular proliferation such as cancer.

IT 477908-99-9P

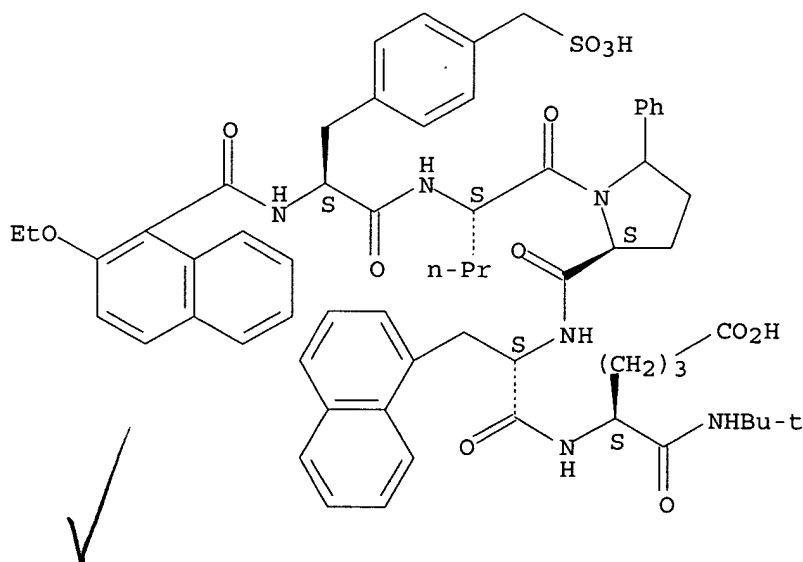
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(method of identifying inhibitors of Cdc25 using three dimensional crystal structure of catalytic domain of Cdc25)

RN 477908-99-9 CAPLUS

CN L-Norvalinamide, N-[(2-ethoxy-1-naphthalenyl)carbonyl]-4-(sulfomethyl)-L-phenylalanyl-L-norvalyl-5-phenyl-L-prolyl-3-(1-naphthalenyl)-L-alanyl-5-carboxy-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 16 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2002:789676 CAPLUS
 DOCUMENT NUMBER: 138:4813

TITLE: Probing Opioid Receptor Interactions with Azacycloalkane Amino Acids. Synthesis of a Potent and Selective ORL1 Antagonist

AUTHOR(S): Halab, Liliane; Becker, Jerome A. J.; Darula, Zsuzsanna; Tourwe, Dirk; Kieffer, Brigitte L.; Simonin, Frederic; Lubell, William D.

CORPORATE SOURCE: Departement de Chimie, Universite de Montreal, Montreal, QC, H3C 3J7, Can.

SOURCE: Journal of Medicinal Chemistry (2002), 45(24), 5353-5357
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 138:4813

AB Four azacycloalkane turn mimics were used to explore the relationship between conformation and biol. activity of peptide ligands to the opioid receptor-like (ORL1) receptor. Three azabicyclo[x.y.0]alkane amino acids and a 5-tBuPro type VI β -turn mimic were introduced into peptides by solid-phase synthesis on MBHA resin. Biol. examination of these peptides showed two new antagonists exhibiting increased selectivity for the ORL1 receptor.

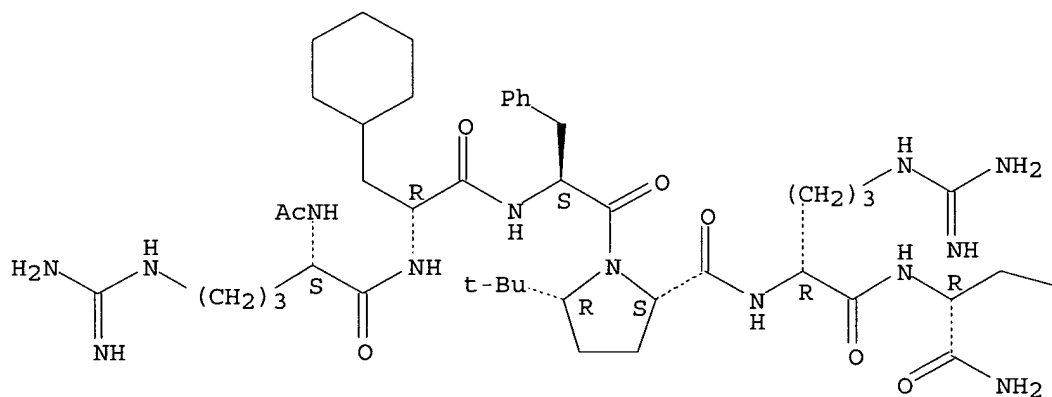
IT **477201-46-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of as ORL1 receptor antagonists via solid-phase peptide synthesis)

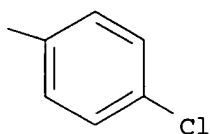
RN 477201-46-0 CAPLUS

CN D-Phenylalaninamide, N2-acetyl-L-arginyl-3-cyclohexyl-D-alanyl-L-phenylalanyl- (5R) -5- (1,1-dimethylethyl) -L-prolyl-D-arginyl-4-chloro- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

151 ANSWER 17 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:777963 CAPLUS

DOCUMENT NUMBER: 137:295254

TITLE: Preparation of peptide inhibitors of hepatitis C virus NS3 protease

INVENTOR(S): Colarusso, Stefania; Gardelli, Cristina; Gerlach, Benjamin; Harper, Steven; Koch, Uwe; Matassa, Victor Giulio; Muraglia, Ester; Narjes, Frank; Ontoria, Ontoria Jesus Maria; Petrocchi, Alessia; Ponzi, Simona; Stansfield, Ian; Summa, Vincenzo

PATENT ASSIGNEE(S): Istituto di Ricerche di Biologia Molecolare P. Angeletti Spa, Italy; et al.

SOURCE: PCT Int. Appl., 151 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2002079234 | A1 | 20021010 | WO 2002-EP3435 | 20020326 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2442540 | AA | 20021010 | CA 2002-2442540 | 20020326 |
| EP 1392721 | A1 | 20040303 | EP 2002-757728 | 20020326 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| US 2004142876 | A1 | 20040722 | US 2004-473443 | 20040303 |
| PRIORITY APPLN. INFO.: | | | GB 2001-7924 | A 20010329 |
| | | | WO 2002-EP3435 | W 20020326 |

OTHER SOURCE(S): MARPAT 137:295254
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Compds. I, II, and III [X = CH₂, O; Y = CRa₂, where Ra = H, OH, CO₂H, alkyl, (hetero)aryl, (hetero)aralkyl, or CRa₂ = cycloalkyl; Z = (un)substituted (hetero)aryl; R₂ = alkyl, fluoroalkyl, or CH₂SH; R₃ = (un)substituted alkyl, (hetero)aryl, (hetero)aralkyl, or together with NRC forms a ring; R_c = H or alkyl or NRC together with R₃ forms a ring; R₄ = alkyl, alkenyl, (hetero)aralkyl, (hetero)aryl or an acidic group; R₅ = (un)substituted carbamoyl, acyl, carboxylic ester, oxalyl, or sulfonyl group, which may be attached to an amino acid or a di- or tripeptide; R₁₃ is a group containing ≤ 25 carbon atoms, 0-5 oxygen atoms, 0-3 nitrogen atoms, 0-2 sulfur atoms and ≤ 9 other heteroatoms which may be the same or different; R₁₇ is H, alkyl, alkenyl, (hetero)aryl, (hetero)aralkyl, OH, alkoxy, aryloxy, (hetero)aralkoxy, thioether, sulfonyl or sulfoxide group; R₁₈ is a group containing ≤ 25 carbon atoms, 0-5 oxygen atoms, 0-3 nitrogen atoms, 0-2 sulfur atoms and ≤ 9 other heteroatoms which may be the same or different] and their pharmaceutically-acceptable salts or esters were prepared as inhibitors of the hepatitis C virus (HCV) NS3 protease. Thus, i-BuO₂C-Glu-Leu-Cys-NHCH₂CH₂C₆H₃Cl₂-2,4 was prepared by the solid-phase method and showed IC₅₀ ≤ 10 μM for inhibition of NS3 protease.

IT 467440-67-1P

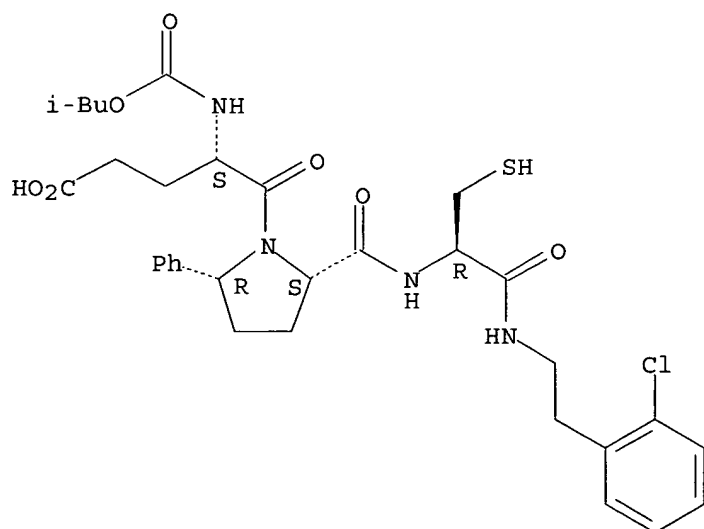
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptide inhibitors of hepatitis C virus NS3 protease)

RN 467440-67-1 CAPLUS

CN L-Cysteinamide, N-[(2-methylpropoxy)carbonyl]-L-α-glutamyl-(5R)-5-phenyl-L-prolyl-N-[2-(2-chlorophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 18 OF 44 CAPLUS COPYRIGHT 2006 ACS on STM

ACCESSION NUMBER: 2002:777885 CAPLUS

DOCUMENT NUMBER: 137:295252

TITLE: Preparation of peptides for pharmaceutical use as modulators of melanocortin receptors

INVENTOR(S): Yu, Guixue; Macor, John; Herpin, Timothy; Lawrence, R. Michael; Morton, George C.; Ruel, Rejean; Poindexter, Graham S.; Ruediger, Edward H.; Thibault, Carl

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 116 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

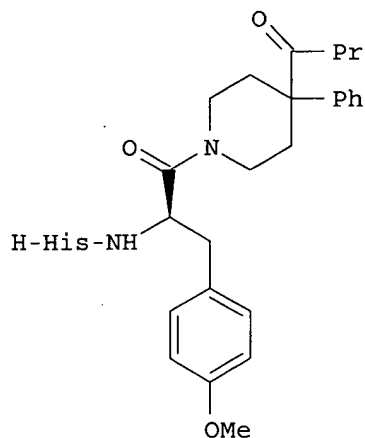
LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|-------------|
| WO 2002079146 | A2 | 20021010 | WO 2002-US6581 | 20020302 |
| WO 2002079146 | A3 | 20030206 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2438272 | AA | 20021010 | CA 2002-2438272 | 20020302 |
| EP 1363631 | A2 | 20031126 | EP 2002-741644 | 20020302 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| JP 2004532838 | T2 | 20041028 | JP 2002-577773 | 20020302 |
| US 2003092732 | A1 | 20030515 | US 2002-90582 | 20020304 |
| US 6979691 | B2 | 20051227 | | |
| US 2003096827 | A1 | 20030522 | US 2002-90288 | 20020304 |
| US 6713487 | B2 | 20040330 | | |
| US 2004229882 | A1 | 20041118 | US 2003-696761 | 20031029 |
| US 2006025403 | A1 | 20060202 | US 2005-199464 | 20050808 |
| PRIORITY APPLN. INFO.: | | | US 2001-273206P | P 20010302 |
| | | | US 2001-273291P | P 20010302 |
| | | | WO 2002-US6581 | W 20020302 |
| | | | US 2002-90288 | A3 20020304 |
| | | | US 2002-90582 | A3 20020304 |
| OTHER SOURCE(S): | MARPAT 137:295252 | | | |
| GI | | | | |



I

AB Compds. $W-(CH_2)_y(CR_4R_5)_xCO-X(R_1)CHR_2(CHR_3)_r(CH_2)_sCO-E$ [$X = N$ or CH ; $R_1, R_3 = H$ or alkyl; $R_2 = H$, aryl, cycloalkyl, heteroaryl, heterocyclyl, (un)substituted alkyl or alkenyl; R_1 together with R_2 or R_3 or R_2 together with R_3 form mono- or bicyclic aryl, cycloalkyl, heteroaryl, or heterocyclyl; $E =$ (un)substituted pyrrolidino, piperidino, or hexahydro-1-azepinyl; $R_4, R_5 = H$, (un)substituted alkyl, halo, hydroxy, amino, aryl, cycloalkyl, heterocyclyl, spirocycloalkyl ring; $r, s = 0$ or 1 ; $x, y = 0-4$; $W =$ amino, carbamoyl, amidino, guanidino, heteroaryl, heterocyclyl, etc.] or their pharmaceutically-acceptable salts or prodrugs were prepared as modulators of melanocortin receptors, particularly MC-1R and MC-4R. Thus, peptide I was prepared by a solution-phase peptide coupling/deprotection scheme.

IT **468105-76-2P 468105-77-3P**

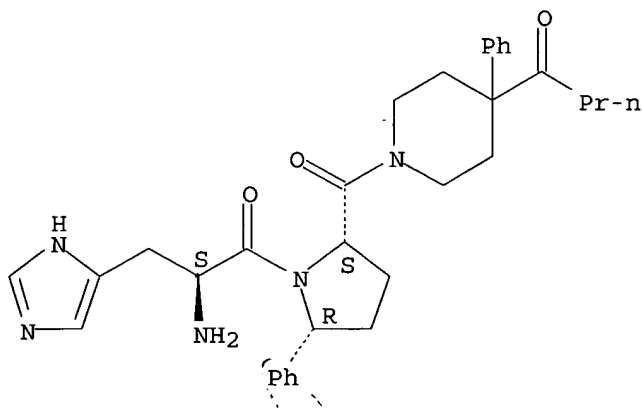
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptides for pharmaceutical use as modulators of melanocortin receptors)

RN 468105-76-2 CAPLUS

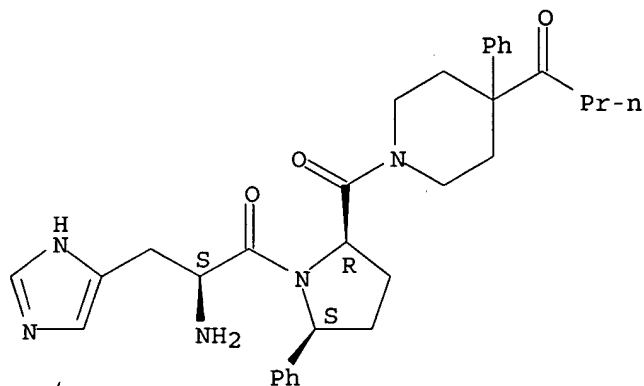
CN Piperidine, 1-[L-histidyl-(5R)-5-phenyl-L-prolyl]-4-(1-oxobutyl)-4-phenyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 468105-77-3 CAPLUS
 CN Piperidine, 1-[L-histidyl-(5S)-5-phenyl-D-prolyl]-4-(1-oxobutyl)-4-phenyl-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



✓ L51 ANSWER 19 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:696111 CAPLUS

DOCUMENT NUMBER: 137:228607

TITLE: Crystal structure and three-dimensional structure of human Cdc25 catalytic domains and its use in designing peptidomimetic inhibitors

INVENTOR(S): Taylor, Neil R.; Borhani, David; Epstein, David; Rudolph, Johannes; Ritter, Kurt; Fujimori, Taro; Robinson, Simon; Eckstein, Jens; Haupt, Andreas; Walker, Nigel; Dixon, Richard W.; Choquette, Deborah; Blanchard, Jill; Kluge, Arthur; Pal, Kollol; Bockovich, Nicholas; Come, Jon; Hediger, Mark

PATENT ASSIGNEE(S): BASF Aktiengesellschaft, Germany; GPC Biotech Inc.

SOURCE: PCT Int. Appl., 351 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2002070680 | A1 | 20020912 | WO 2001-US6587 | 20010301 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: WO 2001-US6587 20010301

OTHER SOURCE(S): MARPAT 137:228607

AB Due to its role in regulating the cell cycle, Cdc25 (a family of dual specificity phosphatases) is a potential target for therapies aimed at

controlling proliferative diseases, but rational, structure-based design has not been possible because of the lack of accurate 3-dimensional data. The present invention relates to polypeptides which comprises the ligand binding domain of human Cdc25 proteins, crystalline forms of these polypeptides, and the use of these crystalline forms to determine the

3-dimensional

structure of the catalytic domain of Cdc25. In particular, a high resolution crystal structure was obtained for the polypeptide denoted CDC25B(Δ N8B), comprising residues Glu-368 through Arg-562 of human Cdc25B, complexed with a pentapeptide inhibitor denoted cdc1249 (2-methoxynaphthyl-1-carboxy-(4-sulfomethyl)-L-Phe-L-Glu-L-Glu-L-naphthylalanine-L-Glu-amide). The invention also relates to the use of the 3-dimensional structure of the Cdc25 catalytic domain in methods of designing and/or identifying potential inhibitors of Cdc25 activity, for example, compds. which inhibit the binding of a native substrate to the Cdc25 catalytic domain. The syntheses and structures of a large number of putative pentapeptide inhibitors are also provided. Such inhibitors have potential in the treatment of diseases associated with excessive cellular proliferation, such as cancer, restenosis, reocclusion of coronary artery, and inflammation.

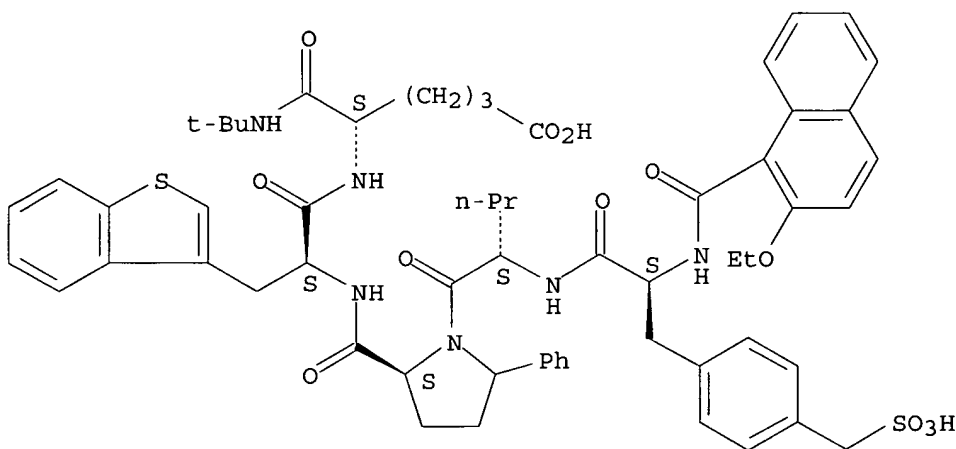
IT 329274-99-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(crystal structure and three-dimensional structure of human Cdc25 catalytic domains and its use in designing peptidomimetic inhibitors)

RN 329274-99-9 CAPLUS

CN L-Norvalinamide, N-[(2-ethoxy-1-naphthalenyl)carbonyl]-4-(sulfomethyl)-L-phenylalanyl-L-norvalyl-5-phenyl-L-prolyl-3-benzo[b]thien-3-yl-L-alanyl-5-carboxy-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

8

THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 20 OR 44

ACCESSION NUMBER:

CAPLUS COPYRIGHT 2006 ACS on STN

2002:695975 CAPLUS

DOCUMENT NUMBER:

137:232913

TITLE:

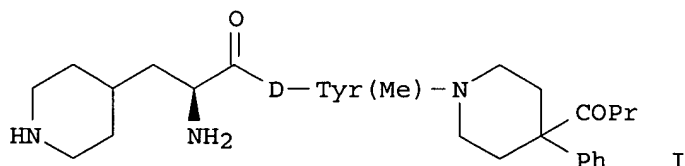
Preparation of peptides for pharmaceutical use as modulators of melanocortin receptors

INVENTOR(S):

Yu, Guixue; Macor, John; Herpin, Timothy; Lawrence, R.

Michael; Morton, George C.; Ruel, Rejean; Poindexter, Graham S.; Ruediger, Edward H.; Thibault, Carl
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
 SOURCE: PCT Int. Appl., 107 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|-------------|
| WO 2002070511 | A1 | 20020912 | WO 2002-US6479 | 20020302 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2437594 | AA | 20020912 | CA 2002-2437594 | 20020302 |
| EP 1363898 | A1 | 20031126 | EP 2002-723310 | 20020302 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| JP 2005511475 | T2 | 20050428 | JP 2002-569831 | 20020302 |
| US 2003092732 | A1 | 20030515 | US 2002-90582 | 20020304 |
| US 6979691 | B2 | 20051227 | | |
| US 2003096827 | A1 | 20030522 | US 2002-90288 | 20020304 |
| US 6713487 | B2 | 20040330 | | |
| US 2004229882 | A1 | 20041118 | US 2003-696761 | 20031029 |
| US 2006025403 | A1 | 20060202 | US 2005-199464 | 20050808 |
| PRIORITY APPLN. INFO.: | | | US 2001-273206P | P 20010302 |
| | | | US 2001-273291P | P 20010302 |
| | | | WO 2002-US6479 | W 20020302 |
| | | | US 2002-90288 | A3 20020304 |
| | | | US 2002-90582 | A3 20020304 |
| OTHER SOURCE(S): | MARPAT 137:232913 | | | |
| GI | | | | |



AB Compds. W-(CR₆R₇)yCH(G)(CR₄R₅)xCO-X(R₁)CHR₂(CHR₃)r(CH₂)sCO-E [X = N or CH; R₁, R₃ = H or alkyl; R₂ = H, aryl, cycloalkyl, heteroaryl, heterocyclyl, (un)substituted alkyl or alkenyl; R₁ together with R₂ or R₃ or R₂ together with R₃ form mono- or bicyclic aryl, cycloalkyl, heteroaryl, or heterocyclyl; E = (un)substituted pyrrolidino, piperidino, hexahydro-1-azepinyl, 1-piperazinyl, cyclopentyl, cyclohexyl, cycloheptyl, amino, (cyclo)alkylamino; R₄-R₆ = H, (un)substituted alkyl, amino, alkylamino, hydroxy, alkoxy, aryl, cycloalkyl, heteroaryl, or

heterocyclyl; or CR4R5 or C6R7 is a spirocycloalkyl ring; r, s = 0 or 1; x = 0-4; y = 0-2; G = alkenyl, arylalkenyl, hydroxy, heteroaryl, cyano, functionalized alkyl or alkenyl, etc.; W = amino, alkylamino, hydroxy, alkoxy, carbamoyl, amidino, cycloalkyl, heteroaryl, heterocyclyl, etc.] were prepared as modulators of melanocortin receptors, particularly MC-1R and MC-4R. Thus, peptide I was prepared by a solution-phase peptide coupling/deprotection scheme.

IT 457894-28-9P 457902-67-9P

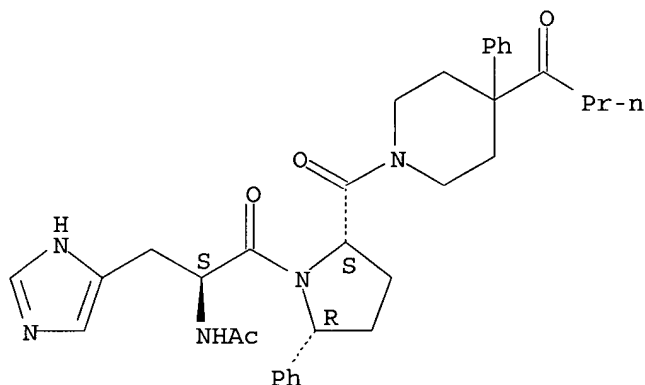
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptides for pharmaceutical use as modulators of melanocortin receptors)

RN 457894-28-9 CAPLUS

CN Acetamide, N-[(1S)-1-(1H-imidazol-4-ylmethyl)-2-oxo-2-[(2S,5R)-2-[[4-(1-oxobutyl)-4-phenyl-1-piperidinyl]carbonyl]-5-phenyl-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

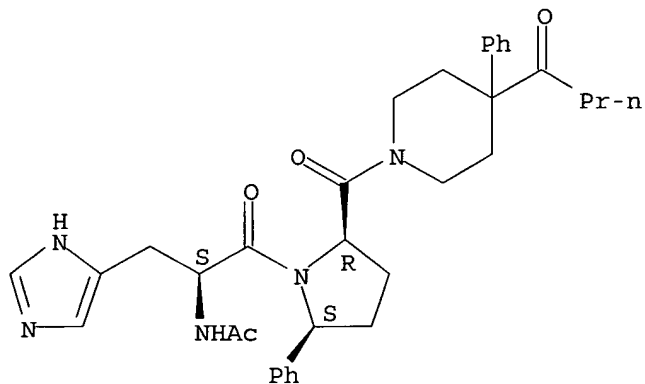
Absolute stereochemistry.



RN 457902-67-9 CAPLUS

CN Acetamide, N-[(1S)-1-(1H-imidazol-4-ylmethyl)-2-oxo-2-[(2R,5S)-2-[[4-(1-oxobutyl)-4-phenyl-1-piperidinyl]carbonyl]-5-phenyl-1-pyrrolidinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

✓ 151 ANSWER 21 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:695727 CAPLUS

DOCUMENT NUMBER: 137:226646

TITLE: Co-administration of melanocortin receptor agonist and phosphodiesterase inhibitor for treatment of cyclic-AMP associated disorders

INVENTOR(S): Macor, John E.; Carlson, Kenneth E.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 91 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|-------------|
| WO 2002069905 | A2 | 20020912 | WO 2002-US6805 | 20020304 |
| WO 2002069905 | A3 | 20031009 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2439691 | AA | 20020912 | CA 2002-2439691 | 20020304 |
| US 2003069169 | A1 | 20030410 | US 2002-90258 | 20020304 |
| EP 1370211 | A2 | 20031217 | EP 2002-713772 | 20020304 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| JP 2005506286 | T2 | 20050303 | JP 2002-569083 | 20020304 |
| US 2004229882 | A1 | 20041118 | US 2003-696761 | 20031029 |
| US 2006025403 | A1 | 20060202 | US 2005-199464 | 20050808 |
| PRIORITY APPLN. INFO.: | | | US 2001-273206P | P 20010302 |
| | | | US 2001-273291P | P 20010302 |
| | | | US 2001-289719P | P 20010509 |
| | | | US 2002-90288 | A3 20020304 |
| | | | US 2002-90582 | A3 20020304 |
| | | | WO 2002-US6805 | W 20020304 |

OTHER SOURCE(S): MARPAT 137:226646

AB Co-administration of a melanocortin receptor agonist, particularly an MC-1R or MC-4R agonist, and a cAMP phosphodiesterase inhibitor is described for modulating levels of cyclic adenosine 3',5' monophosphate (cAMP) in a mammal. The inventive co-administration is useful in the treatment of diseases affected by activity of cAMP-PDE, including without limitation, inflammatory bowel disease, irritable bowel syndrome, rheumatoid arthritis, osteoarthritis, pancreatitis, psoriasis, migraine, Alzheimer's Disease, Parkinson's disease, transplant rejection, asthma, acute respiratory distress syndrome, chronic obstructive pulmonary disease, stroke, and neurodegeneration of, and consequences of traumatic brain injury.

IT 457894-28-9P

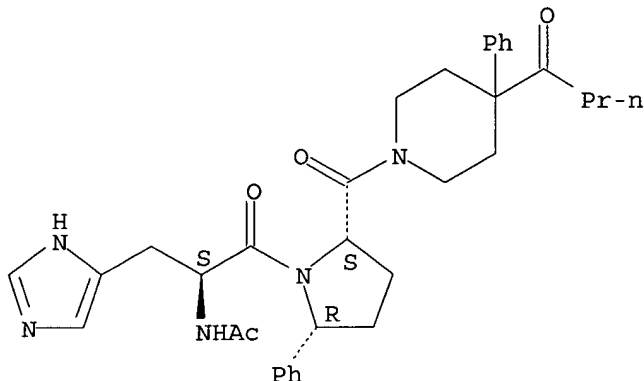
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Co-administration of melanocortin receptor agonist and cAMP phosphodiesterase inhibitor for treatment of cAMP-associated disorders)

RN 457894-28-9 CAPLUS

CN Acetamide, N-[(1S)-1-(1H-imidazol-4-ylmethyl)-2-oxo-2-[(2S,5R)-2-[[4-(1-oxobutyl)-4-phenyl-1-piperidinyl]carbonyl]-5-phenyl-1-pyrrolidinyl]ethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 22 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:130117 CAPLUS

DOCUMENT NUMBER: 136:325819

TITLE: Effect of Sequence on Peptide Geometry in 5-tert-Butylprolyl Type VI β -Turn Mimics

AUTHOR(S): Halab, Liliane; Lubell, William D.

CORPORATE SOURCE: Departement de Chimie, Universite de Montreal, Montreal, QC, H3C 3J7, Can.

SOURCE: Journal of the American Chemical Society (2002), 124(11), 2474-2484

CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 136:325819

AB The influence of sequence on turn geometry was examined by incorporating (2S,5R)-5-tert-butylproline (tBuPro) into a series of dipeptides and tetrapeptides. (2S,5R)-5-Tert-butylproline and proline were resp. introduced at the C-terminal residue of N-acetyl dipeptide N'-methylenamides MeCO-Xaa-Pro-NHMe and MeCO-Xaa-tBuPro-NHMe (Xaa = Ser, Asp, Tyr, Phe, Trp). The conformational anal. of these analogs was performed using NMR and CD spectroscopy as well as x-ray diffraction to examine the factors that control the prolyl amide ("prolyl amide" refers to the tertiary amide composed of the pyrrolidine nitrogen of the prolyl residue and the carbonyl of the N-terminal residue) equilibrium and stabilize type VI β -turn conformation. The high cis-isomer population with aromatic residues N-terminal to proline was shown to result from a stacking interaction between the partial pos. charged prolyl amide nitrogen and the aromatic π -system as seen in the crystal structure of MeCO-Tyr-Pro-NHMe. The effect of sequence on the prolyl amide equilibrium of tBuPro-tetrapeptides,

MeCO-Xaa-Yaa-tBuPro-Zaa-XMe (Xaa = Ala, Ser, Val; Yaa = Ala, Leu, Phe; Zaa = Ala, Leu, Phe, Val, Lys; X = O, NH), was studied. High (>80%) cis-isomer populations were obtained with alkyl groups at the Xaa position, an aromatic residue at the Yaa position, and either an Ala or a Lys at the Zaa position of the tBuPro-tetrapeptide Me esters in water. Tetrapeptides MeCO-Ala-Phe-tBuPro-Zaa-OMe (Zaa = Ala, Lys) with high cis-isomer content adopted type VIa β -turn conformations as shown by their NMR and CD spectra. Although a pattern of amide proton temperature

coefficient

values indicative of a hairpin geometry was observed in the above two peptides, the value magnitudes did not indicate strong hydrogen bonding in water.

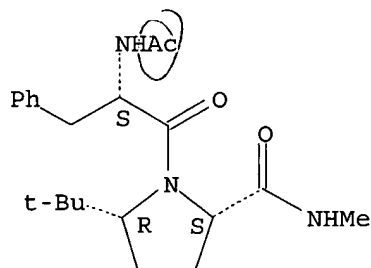
IT 224951-49-9P 412303-12-9P 412303-13-0P
 412303-14-1P 412303-15-2P 412303-16-3P
 412303-28-7P 412303-29-8P 412303-30-1P
 412303-31-2P 412303-32-3P 412303-33-4P
 412303-34-5P 412303-35-6P 412303-36-7P
 412303-37-8P 412303-38-9P 412303-39-0P
 412303-40-3P 412303-41-4P 412303-42-5P
 412303-43-6P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
 (preparation and β -turn conformation anal. of prolyl- or
 tert-butylprolyl-peptides)

RN 224951-49-9 CAPLUS

CN L-Prolinamide, N-acetyl-L-phenylalanyl-5-(1,1-dimethylethyl)-N-methyl-,
 (5R)- (9CI) (CA INDEX NAME)

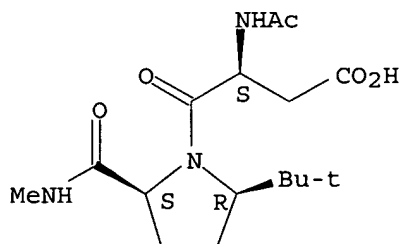
Absolute stereochemistry.



RN 412303-12-9 CAPLUS

CN L-Prolinamide, N-acetyl-L- α -aspartyl-5-(1,1-dimethylethyl)-N-methyl-,
 (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

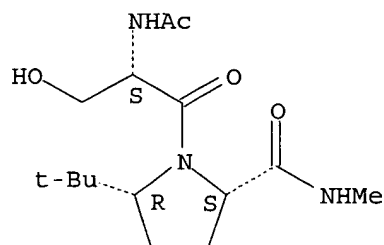


RN 412303-13-0 CAPLUS

CN L-Prolinamide, N-acetyl-L-seryl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-

(9CI) (CA INDEX NAME)

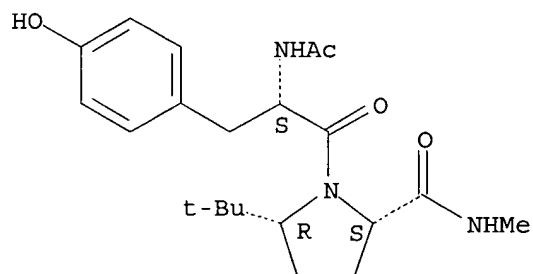
Absolute stereochemistry.



RN 412303-14-1 CAPLUS

CN L-Prolinamide, N-acetyl-L-tyrosyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-
(9CI) (CA INDEX NAME)

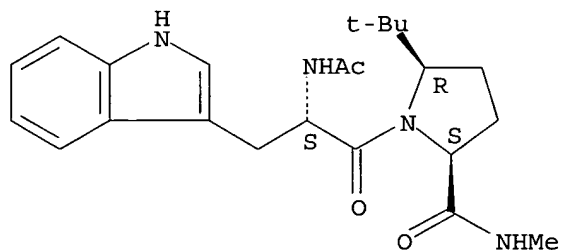
Absolute stereochemistry.



RN 412303-15-2 CAPLUS

CN L-Prolinamide, N-acetyl-L-tryptophyl-5-(1,1-dimethylethyl)-N-methyl-,
(5R)- (9CI) (CA INDEX NAME)

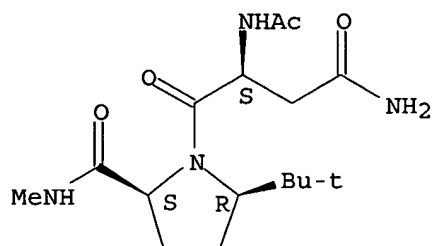
Absolute stereochemistry.



RN 412303-16-3 CAPLUS

CN L-Prolinamide, N2-acetyl-L-asparaginyl-5-(1,1-dimethylethyl)-N-methyl-,
(5R)- (9CI) (CA INDEX NAME)

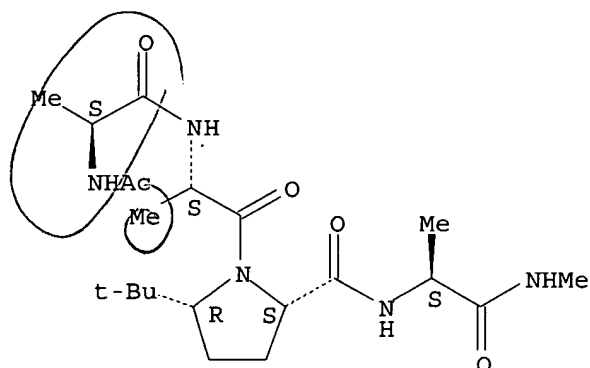
Absolute stereochemistry.



RN 412303-28-7 CAPLUS

CN L-Alaninamide, N-acetyl-L-alanyl-L-alanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-N-methyl- (9CI) (CA INDEX NAME)

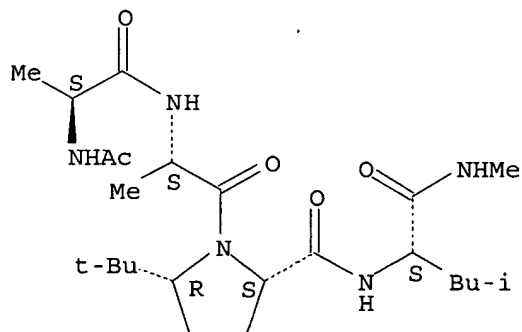
Absolute stereochemistry.



RN 412303-29-8 CAPLUS

CN L-Leucinamide, N-acetyl-L-alanyl-L-alanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-N-methyl- (9CI) (CA INDEX NAME)

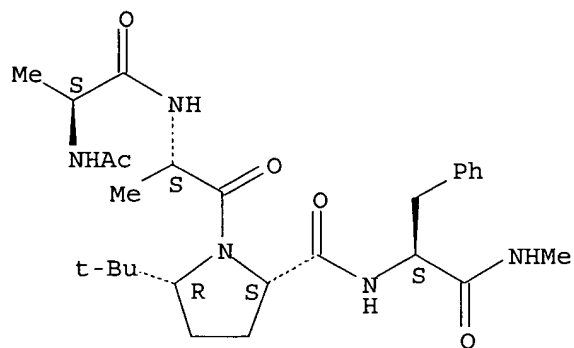
Absolute stereochemistry.



RN 412303-30-1 CAPLUS

CN L-Phenylalaninamide, N-acetyl-L-alanyl-L-alanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-N-methyl- (9CI) (CA INDEX NAME)

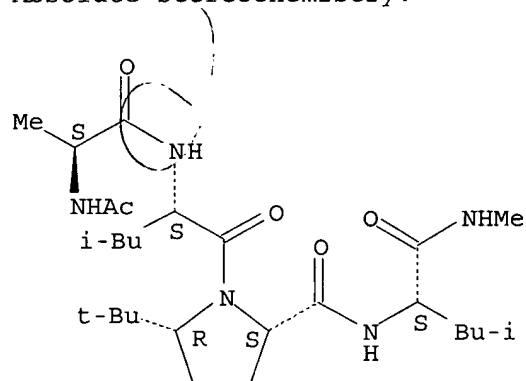
Absolute stereochemistry.



RN 412303-31-2 CAPLUS

CN L-Leucinamide, N-acetyl-L-alanyl-L-leucyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-N-methyl- (9CI) (CA INDEX NAME)

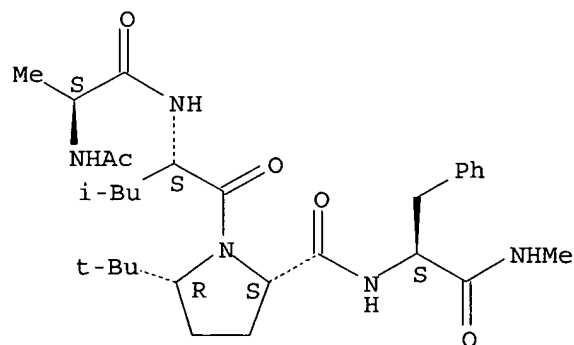
Absolute stereochemistry.



RN 412303-32-3 CAPLUS

CN L-Phenylalaninamide, N-acetyl-L-alanyl-L-leucyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-N-methyl- (9CI) (CA INDEX NAME)

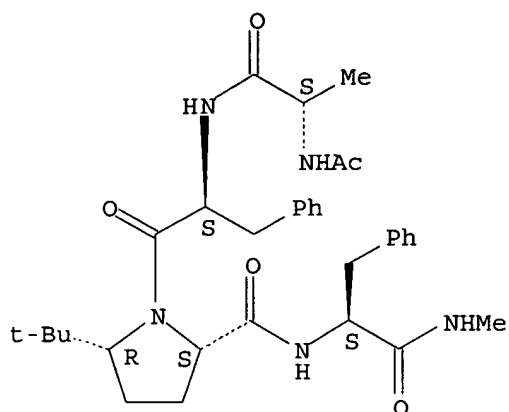
Absolute stereochemistry.



RN 412303-33-4 CAPLUS

CN L-Phenylalaninamide, N-acetyl-L-alanyl-L-phenylalanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-N-methyl- (9CI) (CA INDEX NAME)

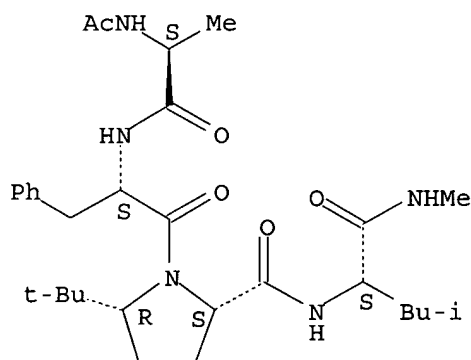
Absolute stereochemistry.



RN 412303-34-5 CAPLUS

CN L-Leucinamide, N-acetyl-L-alanyl-L-phenylalanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-N-methyl- (9CI) (CA INDEX NAME)

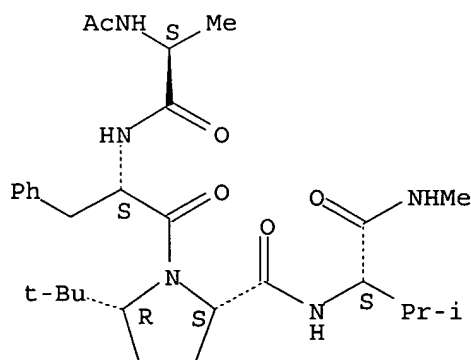
Absolute stereochemistry.



RN 412303-35-6 CAPLUS

CN L-Valinamide, N-acetyl-L-alanyl-L-phenylalanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-N-methyl- (9CI) (CA INDEX NAME)

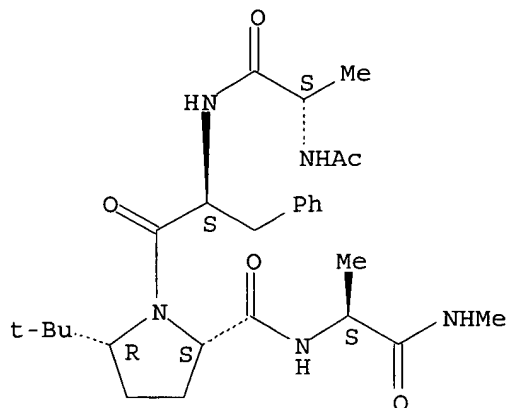
Absolute stereochemistry.



RN 412303-36-7 CAPLUS

CN L-Alaninamide, N-acetyl-L-alanyl-L-phenylalanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-N-methyl- (9CI) (CA INDEX NAME)

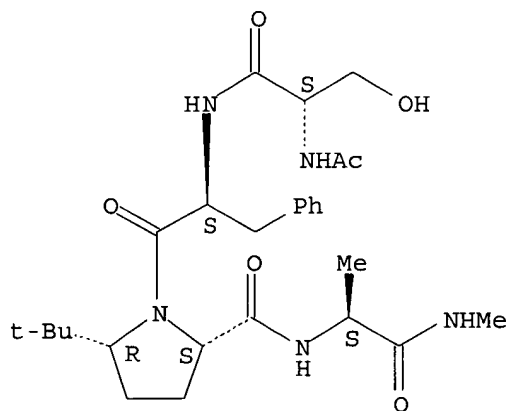
Absolute stereochemistry.



RN 412303-37-8 CAPLUS

CN L-Alaninamide, N-acetyl-L-seryl-L-phenylalanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-N-methyl- (9CI) (CA INDEX NAME)

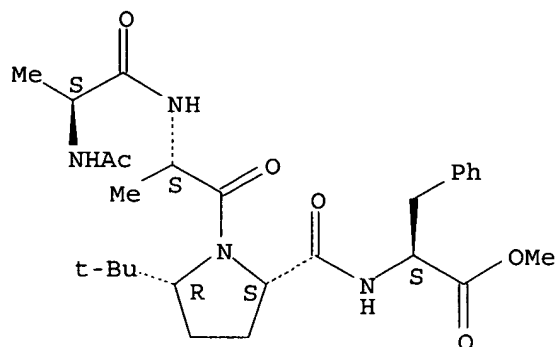
Absolute stereochemistry.



RN 412303-38-9 CAPLUS

CN L-Phenylalanine, N-acetyl-L-alanyl-L-alanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-, methyl ester (9CI) (CA INDEX NAME)

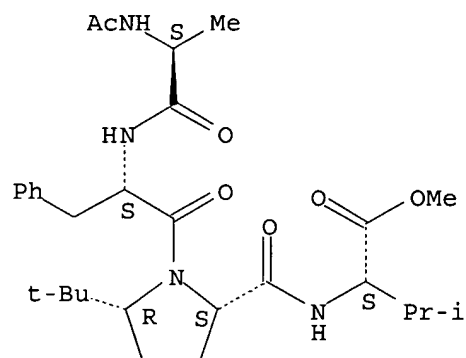
Absolute stereochemistry.



RN 412303-39-0 CAPLUS

CN L-Valine, N-acetyl-L-alanyl-L-phenylalanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-, methyl ester (9CI) (CA INDEX NAME)

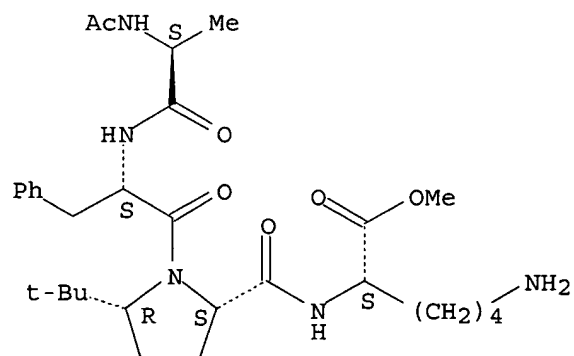
Absolute stereochemistry.



RN 412303-40-3 CAPLUS

CN L-Lysine, N-acetyl-L-alanyl-L-phenylalanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-, methyl ester (9CI) (CA INDEX NAME)

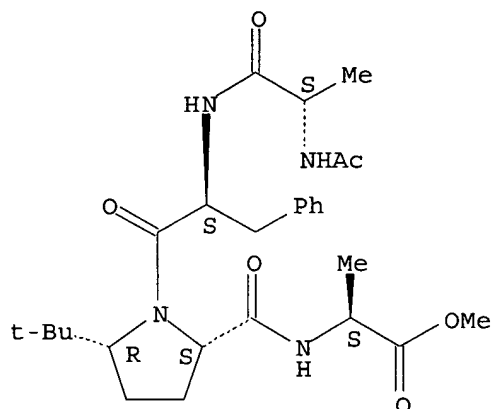
Absolute stereochemistry.



RN 412303-41-4 CAPLUS

CN L-Alanine, N-acetyl-L-alanyl-L-phenylalanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-, methyl ester (9CI) (CA INDEX NAME)

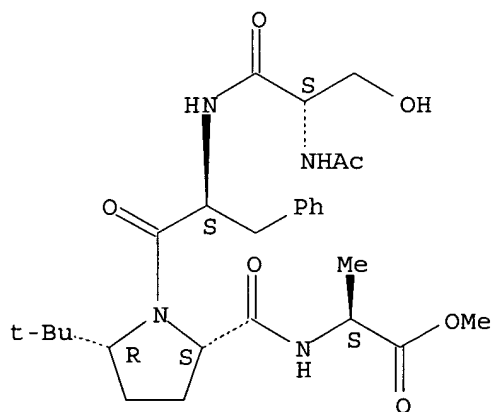
Absolute stereochemistry.



RN 412303-42-5 CAPLUS

CN L-Alanine, N-acetyl-L-seryl-L-phenylalanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-, methyl ester (9CI) (CA INDEX NAME)

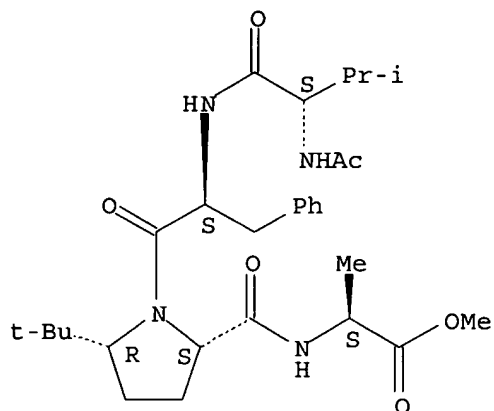
Absolute stereochemistry.



RN 412303-43-6 CAPLUS

CN L-Alanine, N-acetyl-L-valyl-L-phenylalanyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 224951-72-8P 412303-18-5P 412303-19-6P
 412303-20-9P 412303-21-0P 412303-49-2P
 412303-50-5P 412303-51-6P

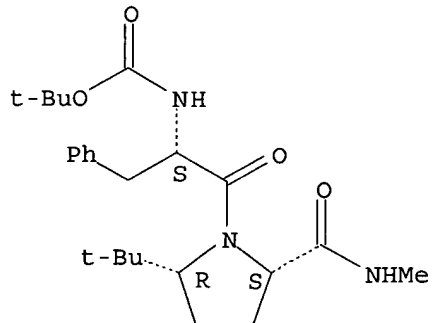
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(preparation and β -turn conformation anal. of prolyl- or
 tert-butylprolyl-peptides)

RN 224951-72-8 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-5-(1,1-
 dimethylethyl)-N-methyl-, (5R)- (9CI) (CA INDEX NAME)

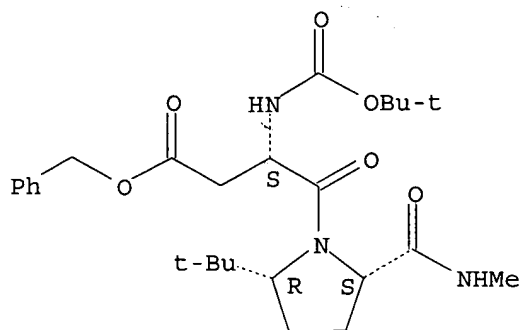
Absolute stereochemistry.



RN 412303-18-5 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-L- α -aspartyl-5-(1,1-
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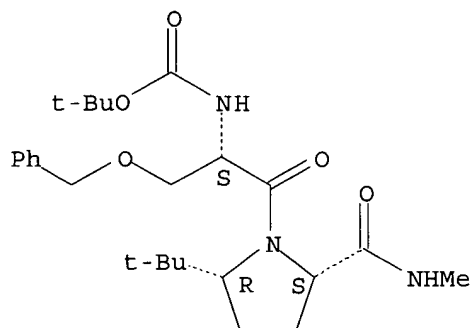
Absolute stereochemistry.



RN 412303-19-6 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-seryl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-(9CI) (CA INDEX NAME)

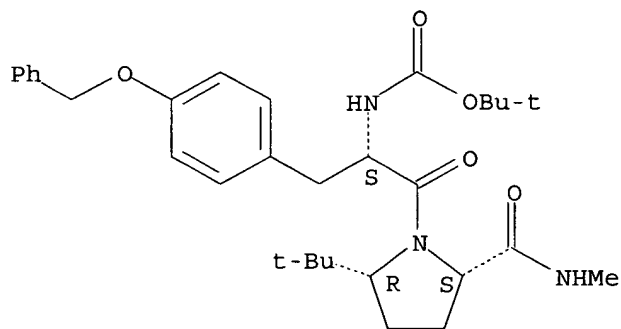
Absolute stereochemistry.



RN 412303-20-9 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-tyrosyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-(9CI) (CA INDEX NAME)

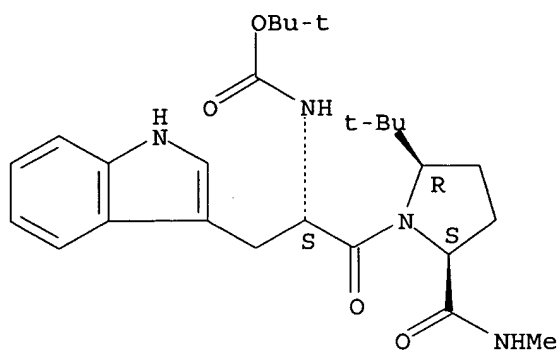
Absolute stereochemistry.



RN 412303-21-0 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-tryptophyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-(9CI) (CA INDEX NAME)

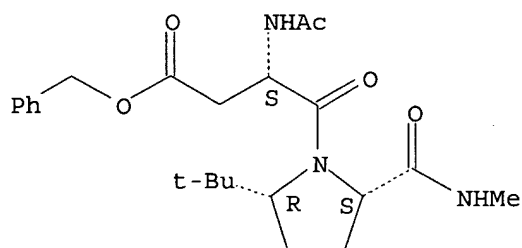
Absolute stereochemistry.



RN 412303-49-2 CAPLUS

CN L-Prolinamide, N-acetyl-L- α -aspartyl-5-(1,1-dimethylethyl)-N-methyl-, phenylmethyl ester, (5R)- (9CI) (CA INDEX NAME)

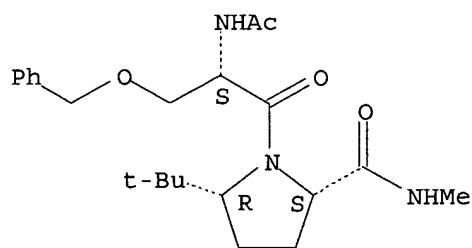
Absolute stereochemistry.



RN 412303-50-5 CAPLUS

CN L-Prolinamide, N-acetyl-O-(phenylmethyl)-L-seryl-5-(1,1-dimethylethyl)-N-methyl-, (5R)- (9CI) (CA INDEX NAME)

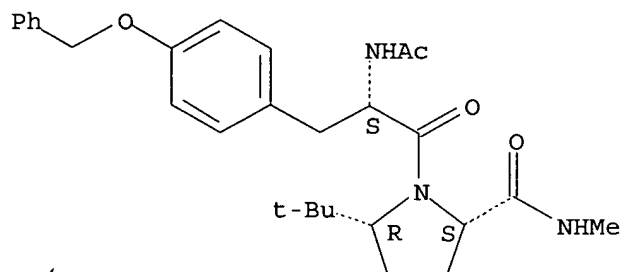
Absolute stereochemistry.



RN 412303-51-6 CAPLUS

CN L-Prolinamide, N-acetyl-O-(phenylmethyl)-L-tyrosyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 23 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:90074 CAPLUS

DOCUMENT NUMBER: 136:151440

TITLE: Preparation of novel peptides as NS3-serine protease inhibitors of hepatitis C virus

INVENTOR(S): Saksena, Anil K.; Girijavallabhan, Viyyoor Moopil; Lovey, Raymond G.; Jao, Edwin E.; Bennett, Frank; McCormick, Jinping; Wang, Haiyan; Pike, Russell E.; Bogen, Stephane L.; Liu, Yi-Tsung; Arasappan, Ashok; Parekh, Tejal; Pinto, Patrick A.; Njoroge, F. George; Ganguly, Ashit K.; Brunck, Terence K.; Kemp, Scott Jeffrey; Levy, Odile Esther; Lim-Wilby, Marguerita

PATENT ASSIGNEE(S): Schering Corporation, USA; Corvas International, Inc.

SOURCE: PCT Int. Appl., 197 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

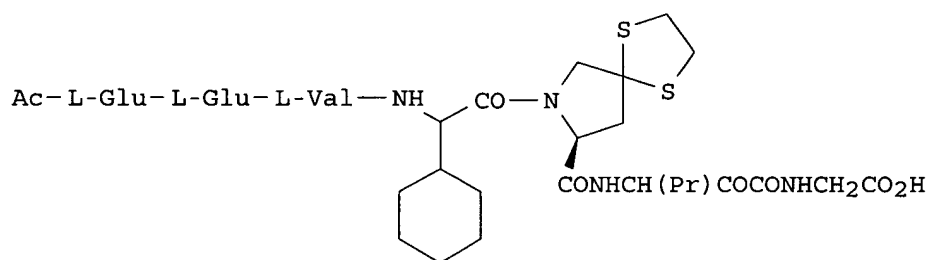
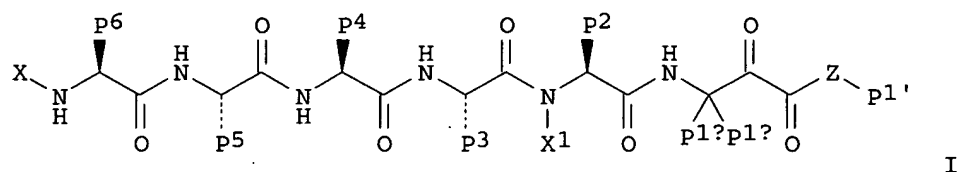
English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|-------------|
| WO 2002008256 | A2 | 20020131 | WO 2001-US22826 | 20010719 |
| WO 2002008256 | A3 | 20020829 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2418204 | AA | 20020131 | CA 2001-2418204 | 20010719 |
| US 2003036501 | A1 | 20030220 | US 2001-909062 | 20010719 |
| US 6800434 | B2 | 20041005 | | |
| EP 1301528 | A2 | 20030416 | EP 2001-959046 | 20010719 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| JP 2004515465 | T2 | 20040527 | JP 2002-514160 | 20010719 |
| US 2005059606 | A1 | 20050317 | US 2004-934141 | 20040903 |
| PRIORITY APPLN. INFO.: | | | US 2000-220109P | P 20000721 |
| | | | US 2001-909062 | A3 20010719 |
| | | | WO 2001-US22826 | W 20010719 |

OTHER SOURCE(S): MARPAT 136:151440
GI



AB Novel peptides I [Z = O, NH or substituted imino; X = (un)substituted alkylsulfonyl, heterocyclisulfonyl, heterocyclialkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylcarbonyl, heterocyclialkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, heterocyclioxy carbonyl, aryloxy carbonyl, heteroaryloxy carbonyl, alkyaminocarbonyl, heterocyclialkylaminocarbonyl, arylaminocarbonyl, or heteroarylaminocarbonyl; X1 = H, alkyl, arylmethyl; P1a, P1b, P2-P6 = H, (un)substituted alkyl, alkenyl, cycloalkyl, heterocyclal, cycloalkylalkyl, heterocyclialkyl, aryl, heteroaryl, arylalkyl, or heteroarylalkyl; P1a and P1b may optionally be joined to each other to form a spirocyclic or spiroheterocyclic ring containing 0-6 oxygen, nitrogen, sulfur, or phosphorus atoms; P1' = H, (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, heterocyclal, heterocyclialkyl, aryl, arylalkyl, heteroaryl, or heteroarylalkyl] having HCV protease inhibitory activity are disclosed. Thus, peptide II was prepared via peptide coupling in solution and showed $K_i = 1-100$ nM for inhibition of HCV protease.

IT 393521-25-0P 393521-27-2P 393521-29-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

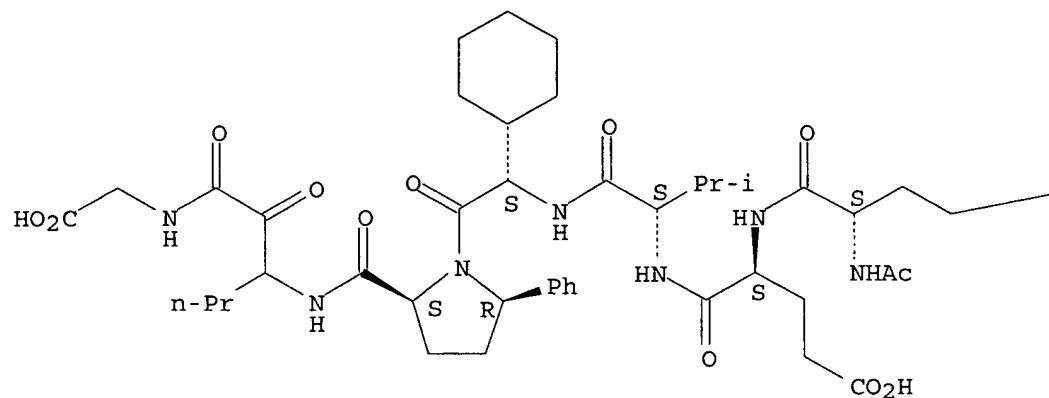
(preparation of novel peptides as NS3-serine protease inhibitors of hepatitis C virus)

RN 393521-25-0 CAPLUS

CN Glycine, N-acetyl-L- α -glutamyl-L- α -glutamyl-L-valyl-(2S)-2-cyclohexylglycyl-(5R)-5-phenyl-L-prolyl-3-amino-2-oxohexanoyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

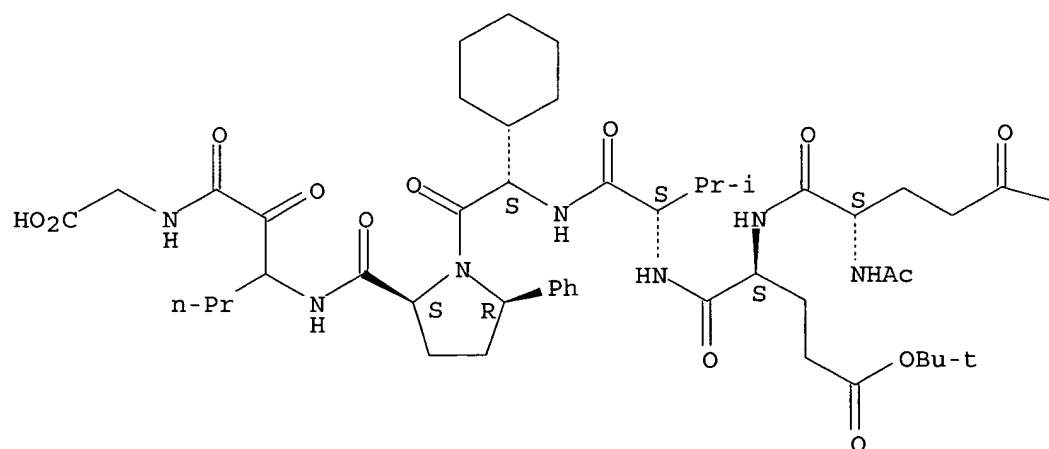
—CO₂H

RN 393521-27-2 CAPLUS

CN Glycine, N-acetyl-L-α-glutamyl-L-α-glutamyl-L-valyl- (2S)-2-cyclohexylglycyl- (5R)-5-phenyl-L-prolyl-3-amino-2-oxohexanoyl-, 1,2-bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

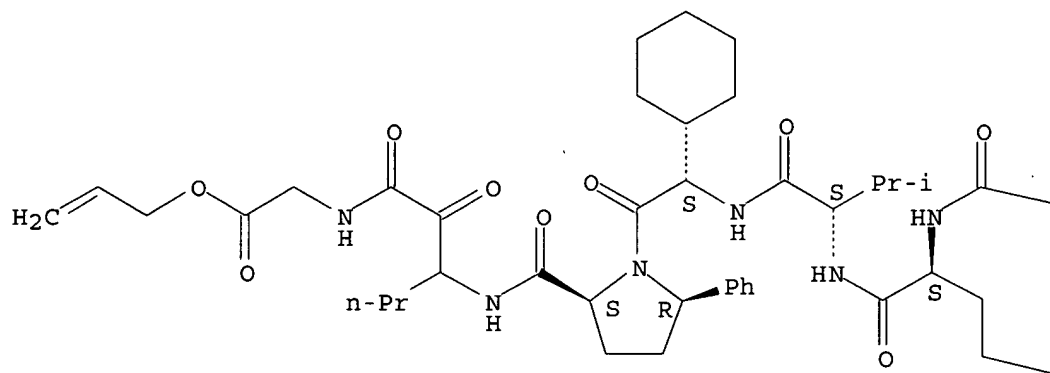
— OBU-t

RN 393521-29-4 CAPLUS

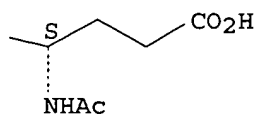
CN Glycine, N-acetyl-L- α -glutamyl-L- α -glutamyl-L-valyl-(2S)-2-cyclohexylglycyl-(5R)-5-phenyl-L-prolyl-3-amino-2-oxohexanoyl-, 7-(2-propenyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



— CO₂H

L51 ANSWER 24 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:90062 CAPLUS

DOCUMENT NUMBER: 136:167698

TITLE: Preparation of peptides as NS3-serine protease inhibitors of hepatitis C virus

INVENTOR(S): Saksena, Anil K.; Girijavallabhan, Viyyoor Moopil; Lovey, Raymond G.; Jao, Edwin E.; Bennett, Frank; McCormick, Jinping L.; Wang, Haiyan; Pike, Russell E.; Bogen, Stephane L.; Chan, Tin-Yau; Liu, Yi-Tsung; Zhu, Zhaoning; Njoroge, F. George; Arasappan, Ashok; Parekh, Tejal N.; Ganguly, Ashit K.; Chen, Kevin X.; Venkatraman, Srikanth; Vaccaro, Henry A.; Pinto, Patrick A.; Santhanam, Bama; Wu, Wanli; Hendrata, Siska; Huang, Yuhua; Kemp, Scott Jeffrey; Levy, Odile Esther; Lim-Wilby, Marguerita; Tamura, Susan Y.

PATENT ASSIGNEE(S): Schering Corporation, USA; Corvas International, Inc.

SOURCE: PCT Int. Appl., 536 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

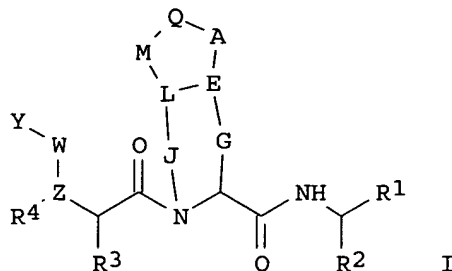
LANGUAGE:

English

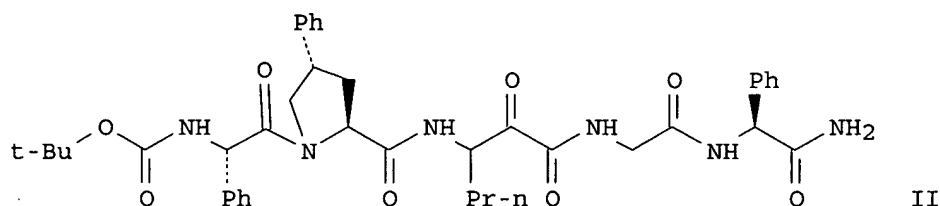
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2002008244 | A2 | 20020131 | WO 2001-US22678 | 20010719 |
| WO 2002008244 | A3 | 20030619 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2410662 | AA | 20020131 | CA 2001-2410662 | 20010719 |
| AU 2001076988 | A5 | 20020205 | AU 2001-76988 | 20010719 |
| BR 2001012540 | A | 20030624 | BR 2001-12540 | 20010719 |
| EP 1385870 | A2 | 20040204 | EP 2001-954764 | 20010719 |
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| JP 2004504404 | T2 | 20040212 | JP 2002-514149 | 20010719 |
| CN 1498224 | A | 20040519 | CN 2001-813111 | 20010719 |
| NZ 523782 | A | 20051028 | NZ 2001-523782 | 20010719 |
| ZA 2002010312 | A | 20040329 | ZA 2002-10312 | 20021219 |
| NO 2003000272 | A | 20030321 | NO 2003-272 | 20030120 |
| PRIORITY APPLN. INFO.: | | | US 2000-220108P | P 20000721 |
| | | | WO 2001-US22678 | W 20010719 |
| OTHER SOURCE(S): | MARPAT 136:167698 | | | |
| GI | | | | |



I



II

AB Peptides I were prepared wherein Y is alkyl, alkyl-aryl, heteroaryl, heteroalkyl, heteroaryl, aryl-heteroaryl, alkylheteroaryl, cycloalkyl, alkyloxy, alkylaryloxy, aryloxy, heteroaryloxy, heterocycloalkyloxy, cycloalkyloxy,, alkylamino, arylamino, alkylarylamino, arylamino, heteroarylamino, cycloalkylamino and heterocycloalkylamino; R1 is acyl, borate; Z is selected from O, N, CH or CR; W, Q, G, J, L, M independently maybe present or absent; W is C=O, C=S, C(=N-CN), or SO; Q is CH, N, P, alkylidene, O, amine, S, or SO; A is O, CH, alkylidene, amine, S, SO or bond; E is CH, N, alkylidene, or double bond; G is alkylidene; J is alkylidene, SO, NH, NR, O; L is CH, alkylidene, O, S or NR; M is O, NR, S, SO, alkylidene; p is 0 to 6; and R-R4 are independently selected from the group consisting of H; alkyl; alkenyl; cycloalkyl; heterocycloalkyl, alkoxy, aryloxy, alkylthio, arylthio, amino, amido, ester, carboxylic acid, carbamate, urea, ketone, aldehyde, cyano, nitro, halogen; (cycloalkyl)alkyl and (heterocycloalkyl)alkyl, which have HCV protease inhibitory activity as well as methods for preparing such compds. In another embodiment, the invention discloses pharmaceutical compns. comprising such compds. as well as methods of using them to treat disorders associated with the HCV protease. Thus peptide II was prepared and tested as antiviral agent and NS3-serine protease inhibitors of hepatitis C virus with Ki ranges in category A = 1-100 nM; category B = 101-1,000 nM; category C > 1000 nM. Also disclosed is the use of I for the manufacture of a medicament for treating HCV, AIDS, and related disorders.

IT 394723-48-9P 394723-49-0P 394723-56-9P
394723-61-6P 394723-62-7P 394727-43-6P
394727-44-7P 394728-85-9P 394730-92-8P
395661-13-9P

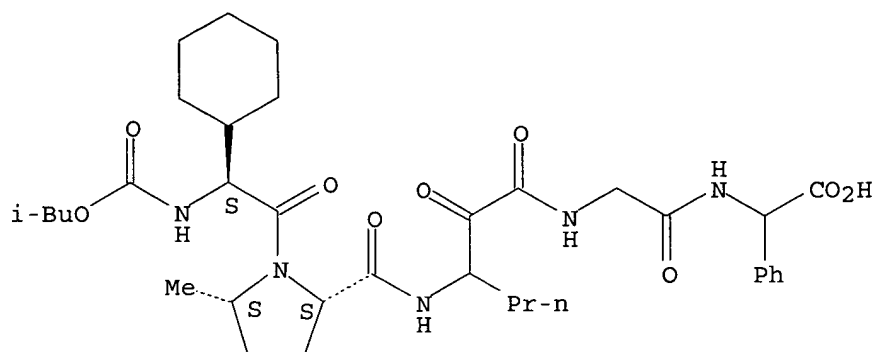
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptides as NS3-serine protease inhibitors of hepatitis C virus)

RN 394723-48-9 CAPLUS

CN Glycine, (2S)-2-cyclohexyl-N-[(2-methylpropoxy)carbonyl]glycyl-(5S)-5-methyl-L-prolyl-3-amino-2-oxohexanoylglycyl-2-phenyl- (9CI) (CA INDEX NAME)

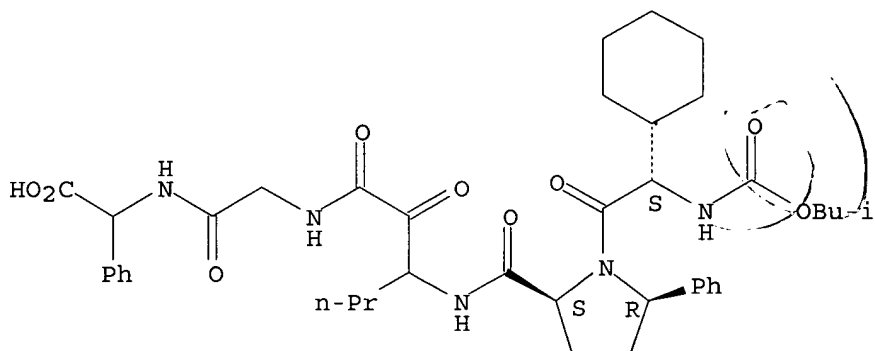
Absolute stereochemistry.



RN 394723-49-0 CAPLUS

CN Glycine, (2S)-2-cyclohexyl-N-[(2-methylpropoxy)carbonyl]glycyl-(5R)-5-phenyl-L-prolyl-3-amino-2-oxohexanoylglycyl-2-phenyl- (9CI) (CA INDEX NAME)

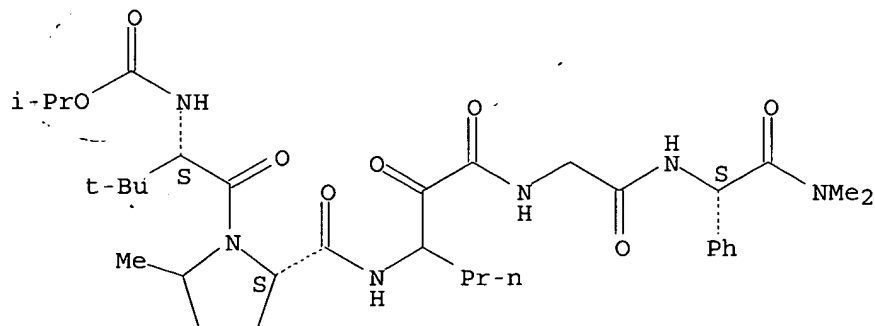
Absolute stereochemistry.



RN 394723-56-9 CAPLUS

CN Glycinamide, 3-methyl-N-[(1-methylethoxy)carbonyl]-L-valyl-4-methyl-L-prolyl-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)- (9CI) (CA INDEX NAME)

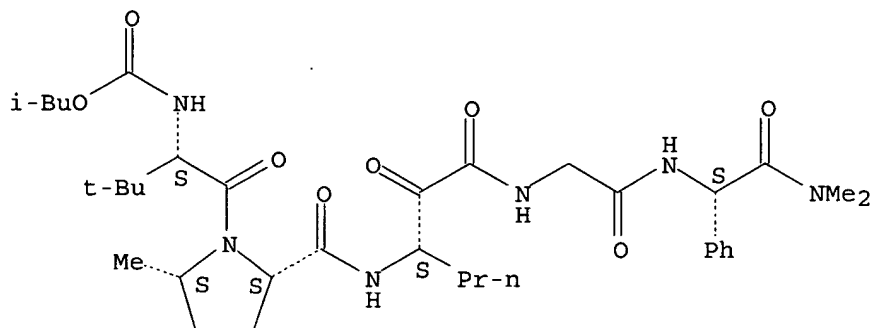
Absolute stereochemistry.



RN 394723-61-6 CAPLUS

CN Glycinamide, 3-methyl-N-[(2-methylpropoxy)carbonyl]-L-valyl-(5S)-5-methyl-L-prolyl-(3S)-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)-(9CI) (CA INDEX NAME)

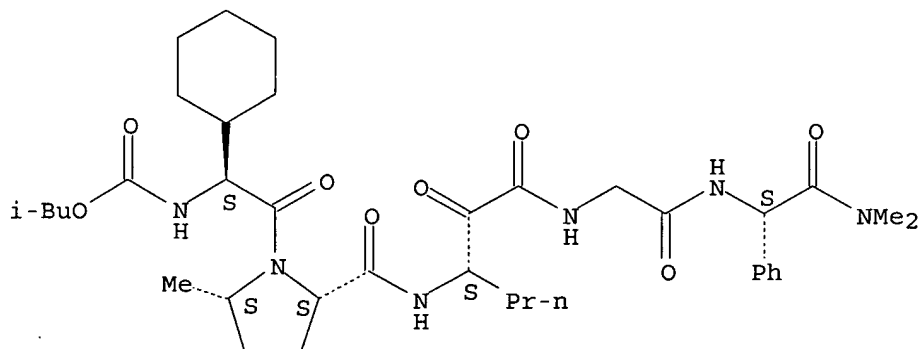
Absolute stereochemistry.



RN 394723-62-7 CAPLUS

CN Glycinamide, (2S)-2-cyclohexyl-N-[(2-methylpropoxy)carbonyl]glycyl-(5S)-5-methyl-L-prolyl-(3S)-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)-(9CI) (CA INDEX NAME)

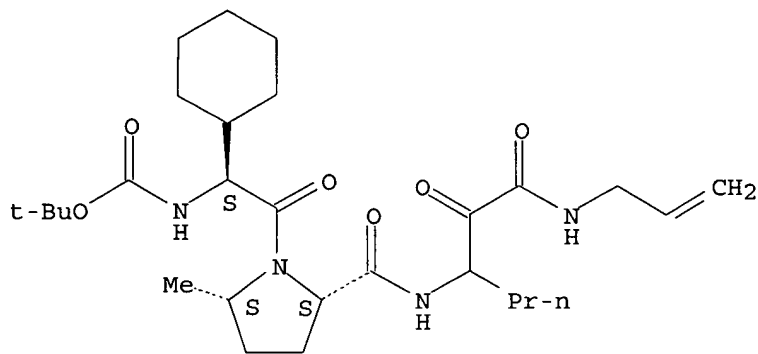
Absolute stereochemistry.



RN 394727-43-6 CAPLUS

CN L-Prolinamide, (2S)-2-cyclohexyl-N-[(1,1-dimethylethoxy)carbonyl]glycyl-5-methyl-N-[1-[oxo(2-propenylamino)acetyl]butyl]-, (5S)-(9CI) (CA INDEX NAME)

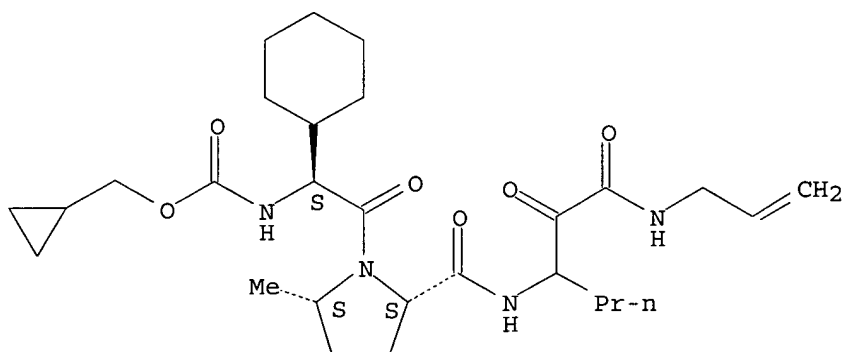
Absolute stereochemistry.



RN 394727-44-7 CAPLUS

CN L-Prolinamide, (2S)-2-cyclohexyl-N-[(cyclopropylmethoxy)carbonyl]glycyl-5-methyl-N-[1-[oxo(2-propenylamino)acetyl]butyl]-, (5S)- (9CI) (CA INDEX NAME)

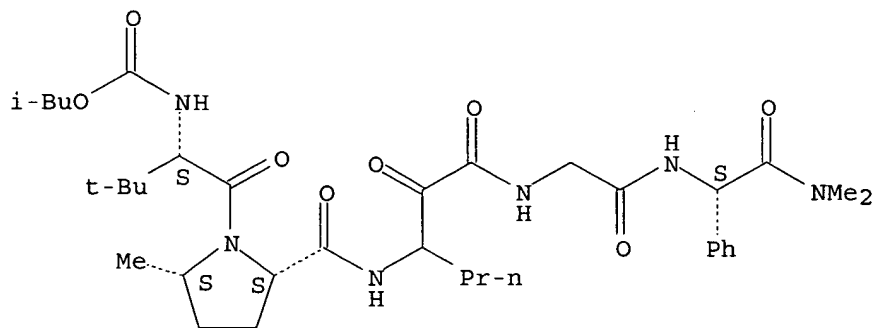
Absolute stereochemistry.



RN 394728-85-9 CAPLUS

CN Glycinamide, 3-methyl-N-[(2-methylpropoxy)carbonyl]-L-valyl-(5S)-5-methyl-L-prolyl-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)- (9CI) (CA INDEX NAME)

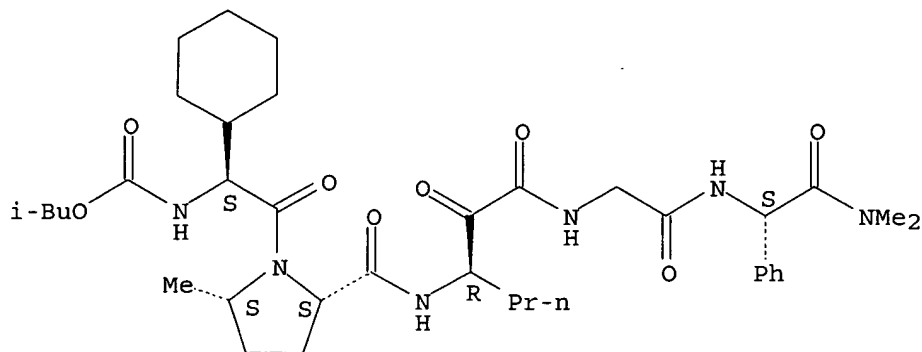
Absolute stereochemistry.



RN 394730-92-8 CAPLUS

CN Glycinamide, (2S)-2-cyclohexyl-N-[(2-methylpropoxy)carbonyl]glycyl-(5S)-5-methyl-L-prolyl-(3R)-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)- (9CI) (CA INDEX NAME)

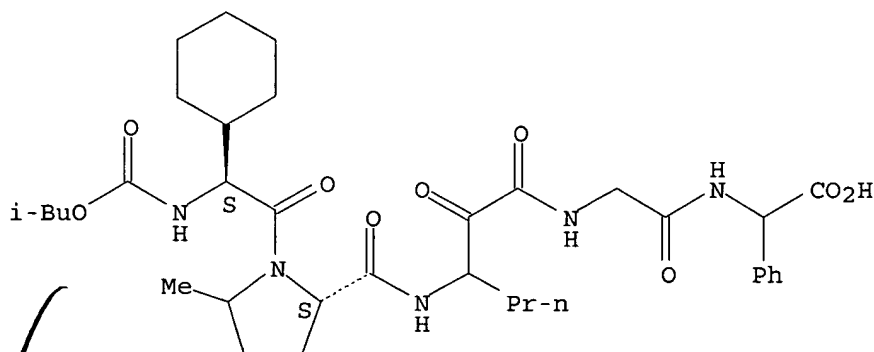
Absolute stereochemistry.



RN 395661-13-9 CAPLUS

CN Glycine, (2S)-2-cyclohexyl-N-[(2-methylpropoxy)carbonyl]glycyl-5-methyl-L-prolyl-3-amino-2-oxohexanoylglycyl-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 25 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:725406 CAPLUS

DOCUMENT NUMBER: 136:86048

TITLE: The influence of steric interactions on the conformation and biology of oxytocin. Synthesis and analysis of penicillamine6-oxytocin and penicillamine6-5-tert-butylproline7-oxytocin analogs
 AUTHOR(S): Belec, L.; Maletinska, L.; Slaninova, J.; Lubell, W. D.

CORPORATE SOURCE: Departement de chimie, Universite de Montreal, Montreal, QC, H3C 3J7, Can.

SOURCE: Journal of Peptide Research (2001), 58(3), 263-273

CODEN: JPERFA; ISSN: 1397-002X

PUBLISHER: Munksgaard International Publishers Ltd.

DOCUMENT TYPE: Journal

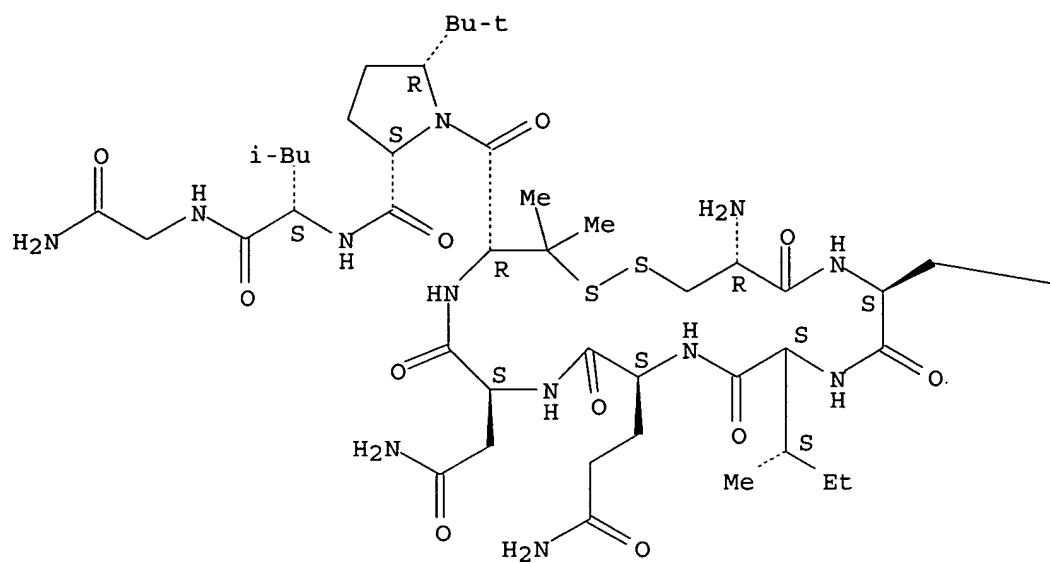
LANGUAGE: English

OTHER SOURCE(S): CASREACT 136:86048

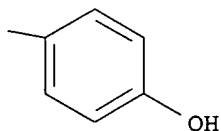
- AB Six [Pen6]oxytocin analogs were synthesized by substituting penicillamine for cysteine in oxytocin, [Mpa1]oxytocin, [dPen1]oxytocin, [5-t-BuPro7]oxytocin, [Mpa1, 5-t-BuPro7]oxytocin and [dPen1, 5-t-BuPro7]oxytocin. When tested in the uterotonic test in vitro [Pen6]oxytocin, [Pen6, 5-t-BuPro7]oxytocin, [Mpa1, Pen6]oxytocin and [Mpa1, Pen6, 5-t-BuPro7]oxytocin, all were found to possess both agonistic and antagonistic properties. Their agonistic potency ranged from negligible (0.08 IU/mg) to low (5.85 IU/mg) and their antagonistic potency (pA2) was estimated to range from 6.6 to 7.9. [DPen1, Pen6]Oxytocin and [dPen1, Pen6, 5-t-BuPro7]oxytocin were found to be pure antagonists with similarly high pA2 values of ≈ 8.2 . Replacement of proline by 5-tert-butylproline increased binding affinity by a factor of two in [Pen6]oxytocin and had no influence on the binding affinity of [Mpa1, Pen6]oxytocin and [dPen1, Pen6]oxytocin. Assignment of the proton signals for prolyl amide cis- and trans-isomers by NMR expts. in water indicated that the Pen6-5-tert-BuPro7 peptide bond cis-isomer population was augmented relative to the prolyl peptides and measured, resp., at 20, 35 and 35% in the 5-tert-butylproline7 analogs of [Pen6]oxytocin, [Mpa1, Pen6]oxytocin and [dPen1, Pen6]oxytocin. This augmentation in cis-isomer population was correlated with a 21-fold reduction in the agonistic potency and 2-fold augmentation in antagonistic potency for [Pen6, 5-t-BuPro7]oxytocin relative to [Pen6]oxytocin. Augmentation of cis-isomer population was also correlated to reduced agonist potency without effect on antagonism on conversion of [Mpa1, Pen6]oxytocin to [Mpa1, Pen6, 5-t-BuPro7]oxytocin. In the potent oxytocin antagonist, [dPen1, Pen6]oxytocin, substitution of 5-tert-butylproline for proline augmented the cis-isomer population without affecting antagonistic potency. The synthesis and evaluation of the [Pen6]oxytocin and [Pen6, 5-t-BuPro7]oxytocin analogs indicated that steric interactions influenced agonist and antagonist activity by modifying peptide conformation. Augmentations in the prolyl cis-isomer population caused by 5-tert-butylproline occurred concurrently with enhanced or maintained antagonistic potency and binding affinity and reduced agonistic potency.
- IT **387868-19-1P 387868-21-5P 387868-23-7P**
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (synthesis and effect of steric interactions on conformation and biol. activity of penicillamine-oxytocin and penicillamine-tert-butylproline-oxytocin analogs)
- RN 387868-19-1 CAPLUS
- CN Glycinamide, L-cysteinyl-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-asparaginy-3-mercapto-L-valyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-L-leucyl-, cyclic (1 \rightarrow 6)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

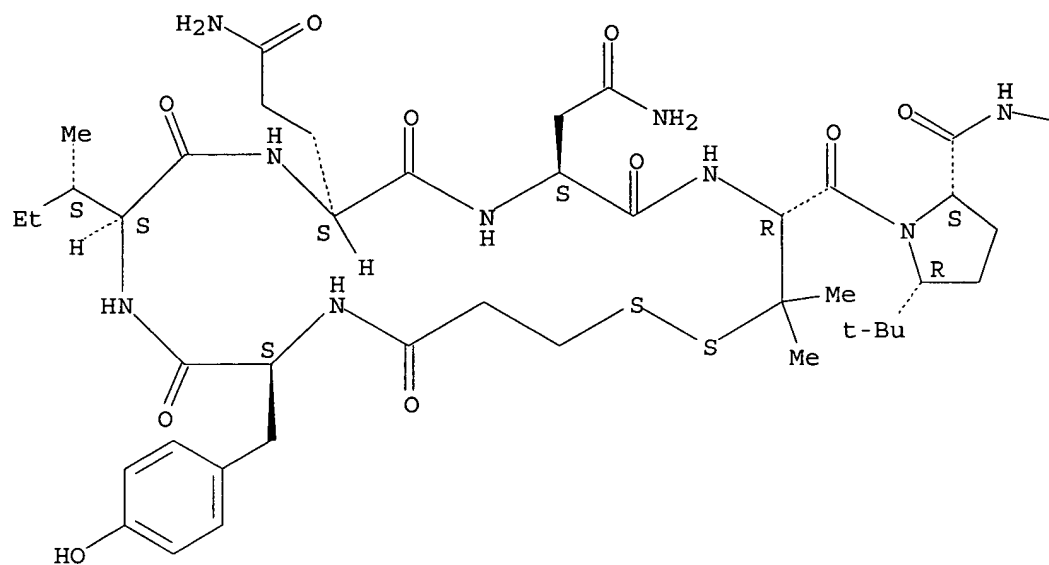


RN 387868-21-5 CAPLUS

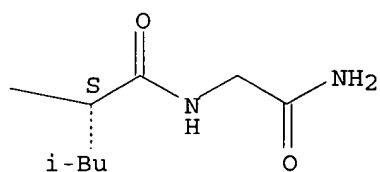
CN Glycinamide, N-(3-mercapto-1-oxopropyl)-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-3-mercapto-L-valyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-L-leucyl-, cyclic (1→5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

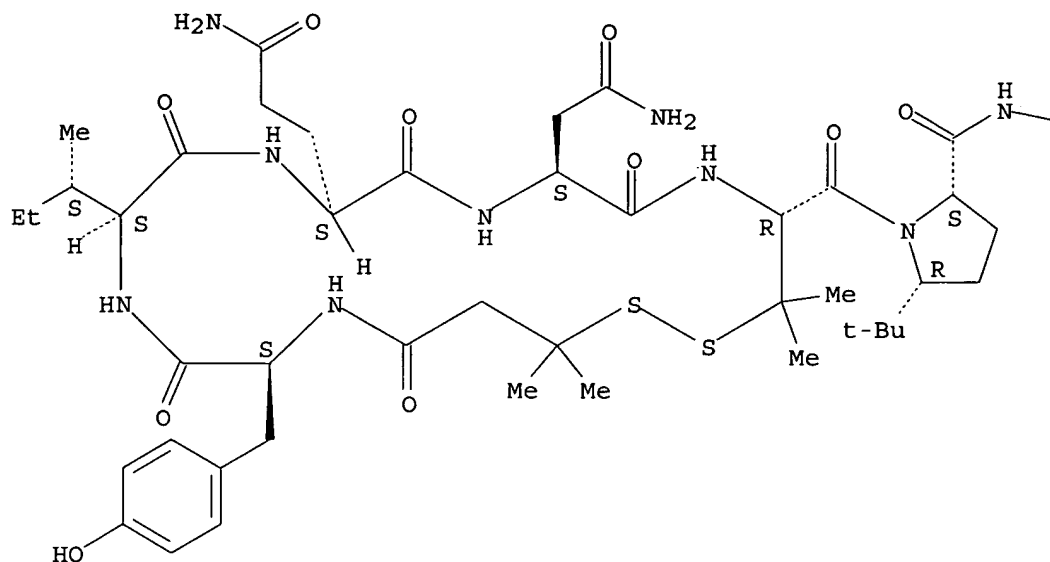


RN 387868-23-7 CAPLUS

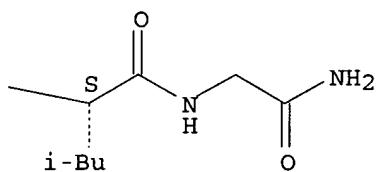
CN Glycinamide, N-(3-mercapto-3-methyl-1-oxobutyl)-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-3-mercapto-L-valyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-L-leucyl-, cyclic (1→5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 387868-28-2P 387868-31-7P 387868-33-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

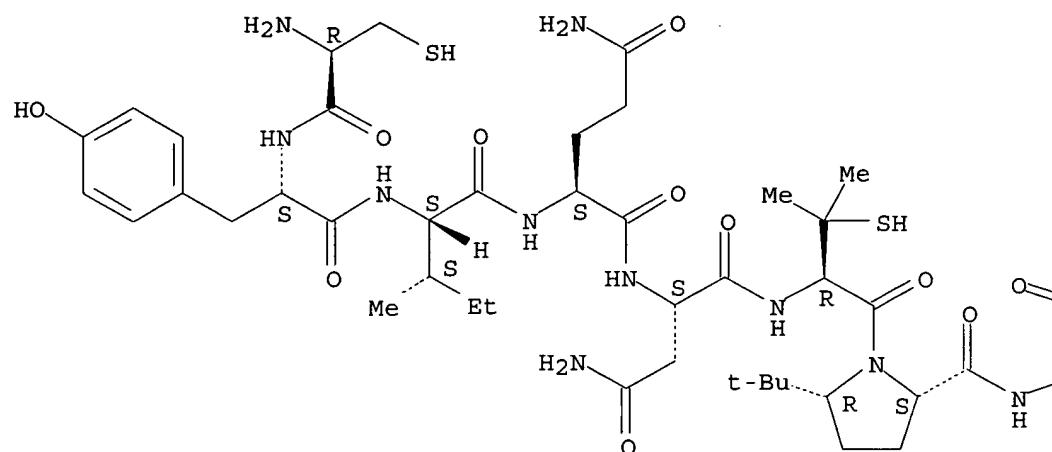
(synthesis and effect of steric interactions on conformation and biol. activity of penicillamine-oxytocin and penicillamine-tert-butylproline-oxytocin analogs)

RN 387868-28-2 CAPLUS

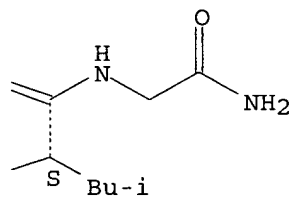
CN Glycinamide, L-cysteinyl-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-3-mercapto-L-valyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-L-leucyl-(9CI)
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

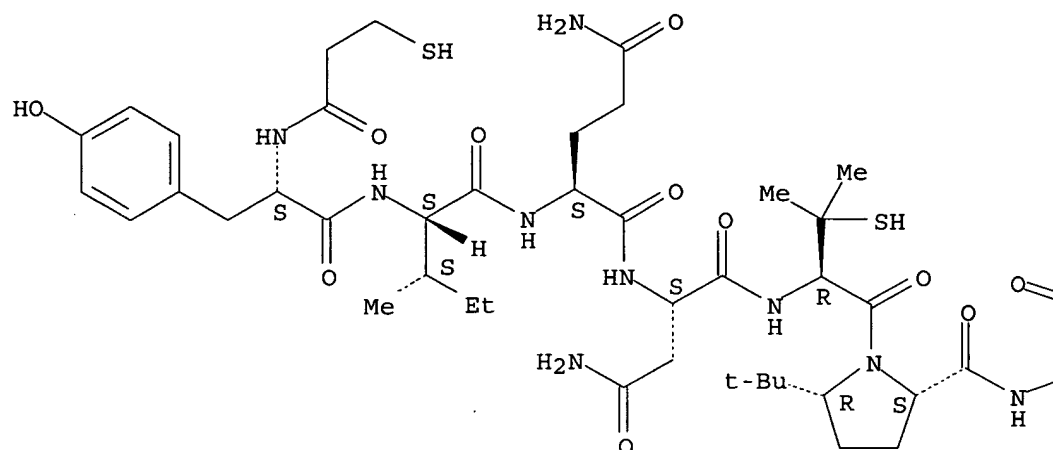


RN 387868-31-7 CAPLUS

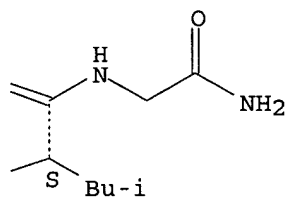
CN Glycinamide, N-(3-mercapto-1-oxopropyl)-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-3-mercapto-L-valyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

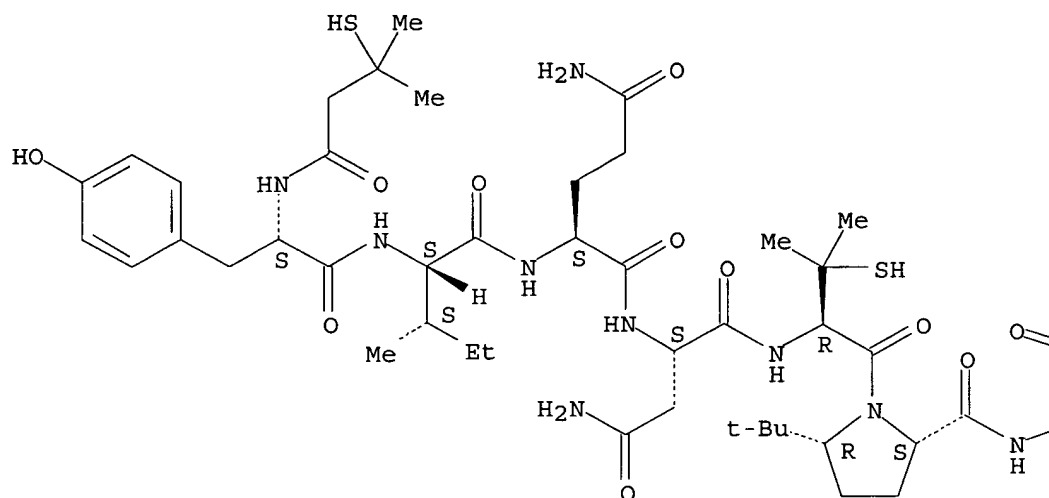


RN 387868-33-9 CAPLUS

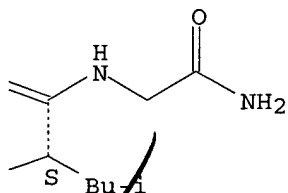
CN Glycinamide, N-(3-mercapto-3-methyl-1-oxobutyl)-L-tyrosyl-L-isoleucyl-L-glutamyl-L-asparaginyl-3-mercaptopropionyl-L-valyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 26 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:250748 CAPLUS

DOCUMENT NUMBER: 135:5807

TITLE: Influence of N-terminal residue stereochemistry on the prolyl amide geometry and the conformation of 5-tert-butylproline type VI β -turn mimics

AUTHOR(S): Halab, Liliane; Lubell, William D.

CORPORATE SOURCE: Departement de chimie, Universite de Montreal, Montreal, QC, H3C 3J7, Can.

SOURCE: Journal of Peptide Science (2001), 7(2), 92-104

CODEN: JPSIEI; ISSN: 1075-2617

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English
 OTHER SOURCE(S): CASREACT 135:5807

AB The effects of N-terminal amino acid stereochem. on prolyl amide geometry and peptide turn conformation were investigated by coupling both L- and D-amino acids to (2S,5R)-5-tert-butylproline and L-proline to generate N-(acetyl)di-peptide N'-methylamides (1 and 2, resp.). Prolyl amide cis- and trans-isomers were, resp., favored for peptides 1 and 2 as observed by proton NMR spectroscopy in water, DMSO and chloroform. The influence of solvent composition on amide proton chemical shift indicated an intramol. hydrogen

bond between the N'-methylamide proton and the acetamide carbonyl for the major conformer of dipeptides (S)-1, that became less favorable in (R)-1 and -2. The coupling constant ($3J_{NH,\alpha}$) values for the cis-isomer of (R)-1 indicated a ϕ_2 dihedral angle value characteristic of a type VIb β -turn conformation in solution X-ray crystallog. anal. of N-acetyl-D-leucyl-5-tert-butylproline N'-methylamide [(R)-1b] showed the prolyl residue in a type VIb β -turn geometry possessing an amide cis-isomer and ψ_3 -dihedral angle having a value of 157° , which precluded an intramol. hydrogen bond. Intermol. hydrogen bonding between the leucyl residues of two turn structures within the unit cell positioned the N-terminal residue in a geometry where their ϕ_2 and ψ_2 dihedral angle values were not characteristic of an ideal type VIb turn. The CD spectra of tert-butylprolyl peptides (S)- and (R)-1b were found not to be influenced by changes in solvent composition from water to acetonitrile. The type B spectrum exhibited by (S)-1b has been previously assigned to a type VIa β -turn conformation. The type C spectrum exhibited by the (R)-1b has previously been associated with type II' β -turn and α -helical conformations in solution and appears now to be also characteristic for a type VIb geometry.

IT 224951-42-2 224951-47-7 224951-49-9

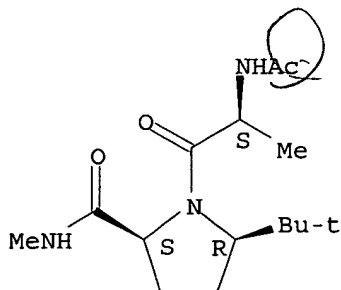
RL: PRP (Properties)

(effect of N-terminal residue stereochem. on prolyl amide geometry and conformation of tert-butylproline type VI β -turn mimics)

RN 224951-42-2 CAPLUS

CN L-Prolinamide, N-acetyl-L-alanyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-(9CI) (CA INDEX NAME)

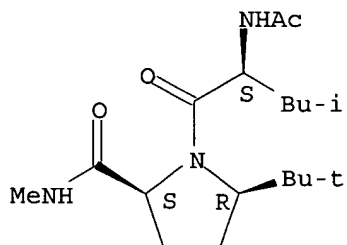
Absolute stereochemistry.



RN 224951-47-7 CAPLUS

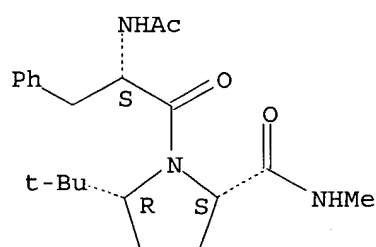
CN L-Prolinamide, N-acetyl-L-leucyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



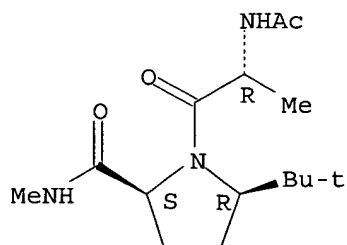
RN 224951-49-9 CAPLUS
 CN L-Prolinamide, N-acetyl-L-phenylalanyl-5-(1,1-dimethylethyl)-N-methyl-,
 (5R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



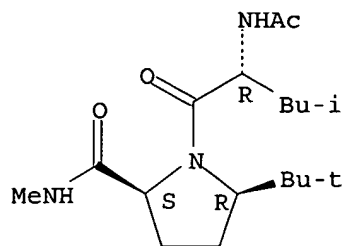
IT 329954-35-0P 329954-38-3P 329954-41-8P
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 (effect of N-terminal residue stereochem. on prolyl amide geometry and
 conformation of tert-butylproline type VI β -turn mimics)
 RN 329954-35-0 CAPLUS
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 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



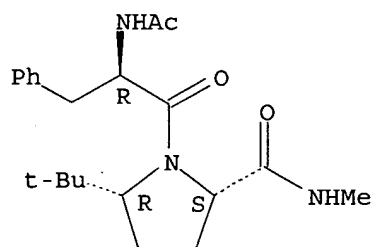
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 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



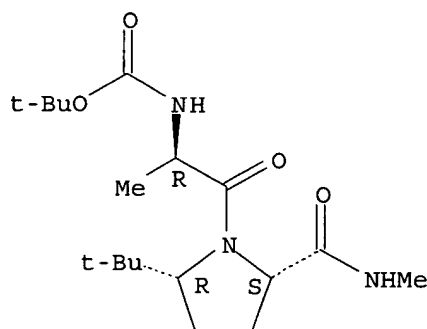
RN 329954-41-8 CAPLUS
 CN L-Prolinamide, N-acetyl-D-phenylalanyl-5-(1,1-dimethylethyl)-N-methyl-,
 (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



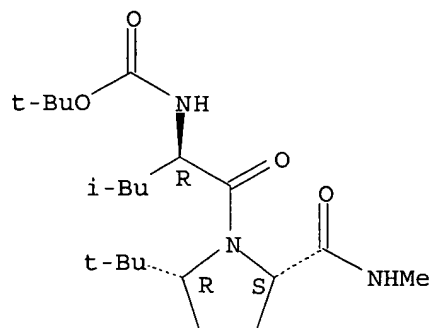
IT 340792-20-3P 340792-23-6P 340792-26-9P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (effect of N-terminal residue stereochem. on prolyl amide geometry and
 conformation of tert-butylproline type VI β -turn mimics)
 RN 340792-20-3 CAPLUS
 CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-D-alanyl-5-(1,1-
 dimethylethyl)-N-methyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 340792-23-6 CAPLUS
 CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-D-leucyl-5-(1,1-
 dimethylethyl)-N-methyl-, (5R)- (9CI) (CA INDEX NAME)

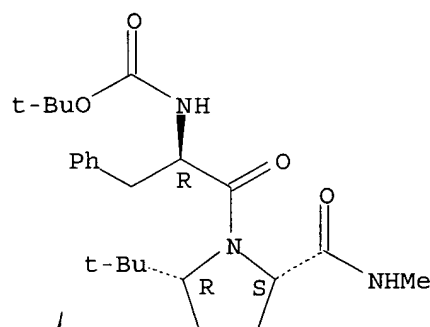
Absolute stereochemistry.



RN 340792-26-9 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-D-phenylalanyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

✓ 51 ANSWER 27 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:168124 CAPLUS

DOCUMENT NUMBER: 134:218936

TITLE: Crystal structure of CDC25 proteins and its use in rational design of inhibitors

INVENTOR(S): Taylor, Neil R.; Borhani, David; Epstein, David; Rudolph, Johannes; Ritter, Kurt; Fujimori, Taro; Robinson, Simon; Eckstein, Jens; Haupt, Andreas; Walker, Nigel; Dixon, Richard W.; Choquette, Deborah; Blanchard, Jill; Kluge, Arthur; Pal, Kollol; Bockovich, Nicholas; Come, Jon; Hediger, Mark

PATENT ASSIGNEE(S): Basf Aktiengesellschaft, Germany

SOURCE: PCT Int. Appl., 314 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2001016300 | A2 | 20010308 | WO 2000-US23473 | 20000825 |

WO 2001016300 A3 20020530

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
 HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
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 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
 YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2383603 AA 20010308 CA 2000-2383603 20000825

EP 1226237 A2 20020731 EP 2000-959449 20000825

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.: US 1999-172215P P 19990831
 WO 2000-US23473 W 20000825

OTHER SOURCE(S): MARPAT 134:218936

AB The present invention relates to polypeptides which comprise the ligand binding domain of CDC25, crystalline forms of these polypeptides, and the use of these crystalline forms to determine the 3-dimensional structure of the catalytic

domain of CDC25 alone and in complexes with pentapeptide inhibitors. Atomic coordinates are provided from x-ray diffraction of crystals of CDC25A and CDC25B catalytic domains in the presence and absence of various inhibitors. The invention also relates to the use of the 3-dimensional structure of the CDC25 catalytic domain in methods of designing and/or identifying potential inhibitors of CDC25 activity, for example, compds. which inhibit the binding of a native substrate to the CDC25 catalytic domain. The method comprises the steps of (1) identifying one or more functional groups capable of interacting with one or more subsites of the CDC25 catalytic domain, and (2) identifying a scaffold which presents the functional group or functional groups in a suitable orientation for interacting with one or more subsites of the CDC25 catalytic domain. Since CDC25 is a potential target for therapies aimed at controlling proliferative disease, the atomic coordinates allow rational structure-based design of potential agents for the treatment of cancer, restenosis, reocclusion of coronary artery, or inflammation.

IT 329274-99-9P

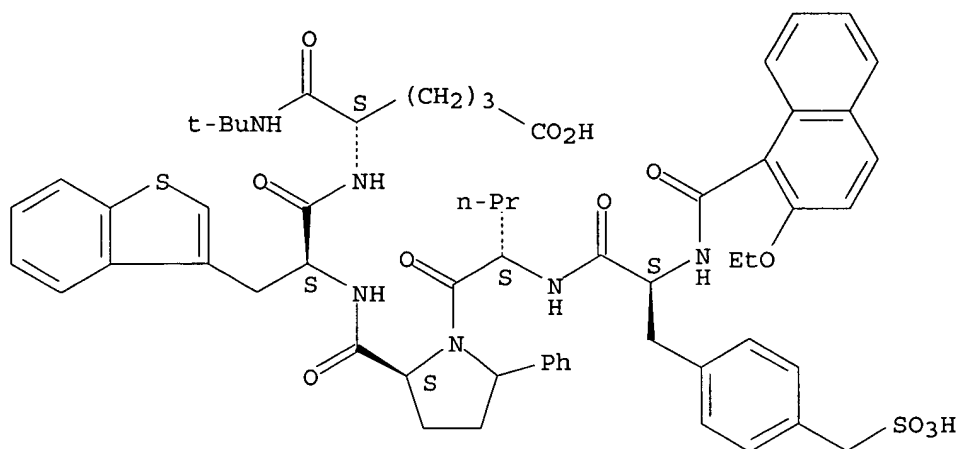
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(crystal structure of CDC25 proteins and its use in rational design of inhibitors)

RN 329274-99-9 CAPLUS

CN L-Norvalinamide, N-[(2-ethoxy-1-naphthalenyl)carbonyl]-4-(sulfomethyl)-L-phenylalanyl-L-norvalyl-5-phenyl-L-prolyl-3-benzo[b]thien-3-yl-L-alanyl-5-carboxy-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 28 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:894780 CAPLUS

DOCUMENT NUMBER: 134:141917

TITLE: Studying the influence of prolyl amide geometry on

AUTHOR(S): Belec, Laurent; Slaninova, Jirina; Lubell, William D.

CORPORATE SOURCE: Departement de chimie, Universite de Montreal,
Montreal, QC, H3C 3J7, Can.

SOURCE: Peptides for the New Millennium, Proceedings of the
American Peptide Symposium, 16th, Minneapolis, MN,
United States, June 26-July 1, 1999 (2000), Meeting
Date 1999, 630-631. Editor(s): Fields, Gregg B.; Tam,
James P.; Barany, George. Kluwer Academic Publishers:
Dordrecht, Neth.

CODEN: 69ATHX

DOCUMENT TYPE: Conference

LANGUAGE: English

AB Three oxytocin (TO) analogs were synthesized in which (2S,5R)-5-t-butylproline was substituted for proline in OT, [Mpa1]-OT (potent agonist) and [dPen1]-OT (potent antagonist). The percent of cis-isomer was 35% for [5-t-BuPro7]-OT, 30% for [Mpa1,5-t-BuPro7]-OT and 20% for [dPen1,5-t-BuPro7]-OT. The peptides were tested for their uterotonic activity in vitro using oxytocin as standard. The two agonist analogs, [5-t-BuPro7]-OT and [Mpa1, 5-t-BuPro7]-OT showed resp. 440 and 70 times weaker binding affinity than OT. Their biol. activities were 200 and 100 times weaker than their proline counterparts. The anal. of these three [5-t-BuPro7]-OT analogs provides addnl. support for the hypothesis concerning the relationship between prolyl amide geometry and uterotonic activity. The moderate augmentation of the cis-isomer population on introduction of 5-t-butylproline stimulated us to investigate a series of [Pen6,5-t-BuPro7]-OT analogs, because the greater steric interaction between the β,β -di-Me cysteine and the 5-t-butylproline residues is expected to enhance further the cis-isomer population.

IT 323192-85-4P 323192-86-5P 323192-87-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

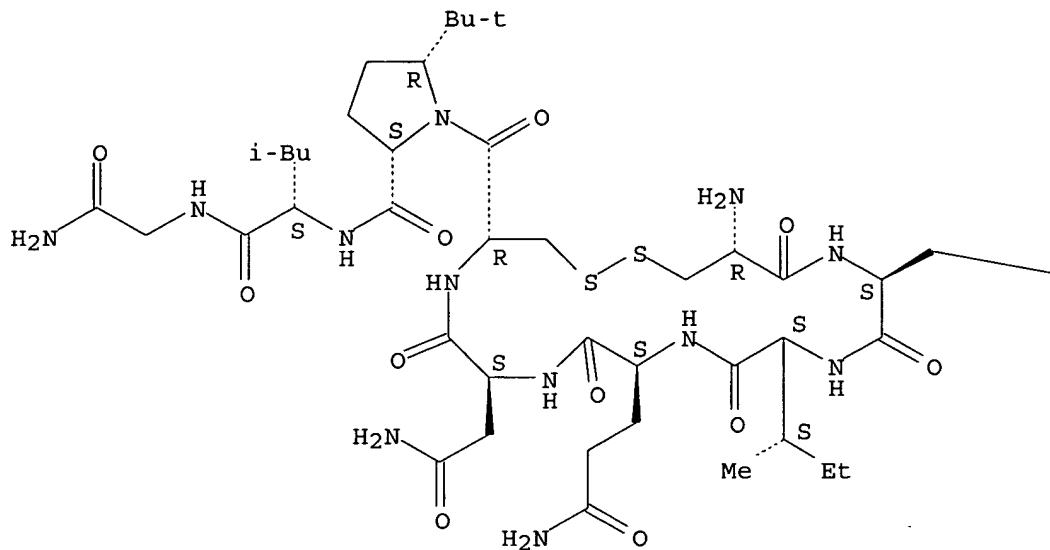
(studying influence of prolyl amide geometry on bioactivity with 5-t-butylproline oxytocin analogs)

RN 323192-85-4 CAPLUS

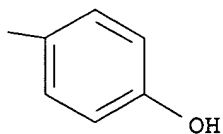
CN Oxytocin, 7-[(5R)-5-(1,1-dimethylethyl)-L-proline]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

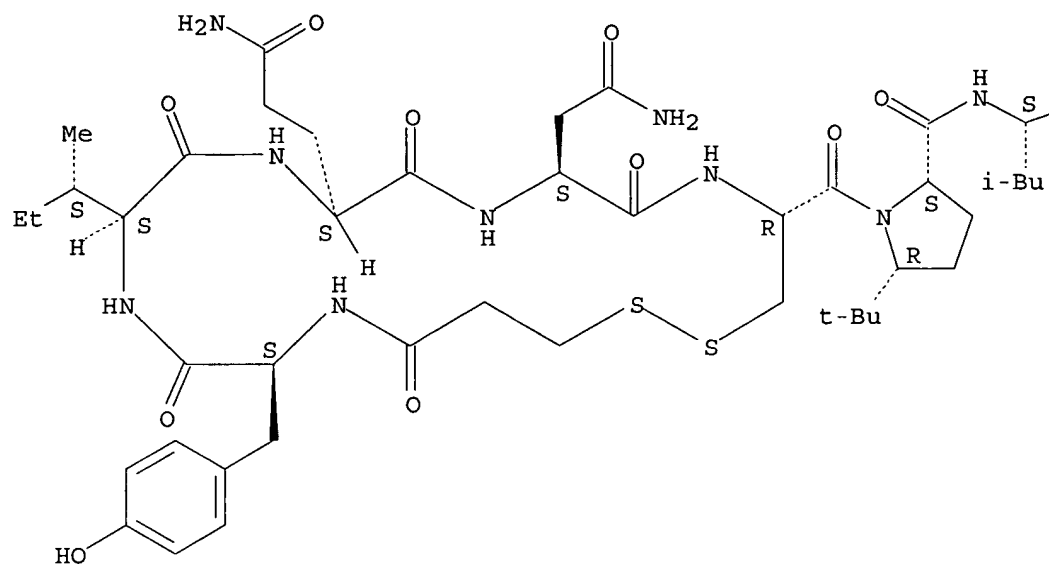


RN 323192-86-5 CAPLUS

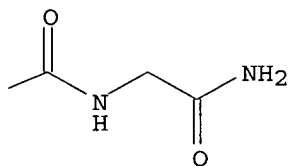
CN Glycinamide, N-(3-mercapto-1-oxopropyl)-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-L-leucyl-, cyclic (1→5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

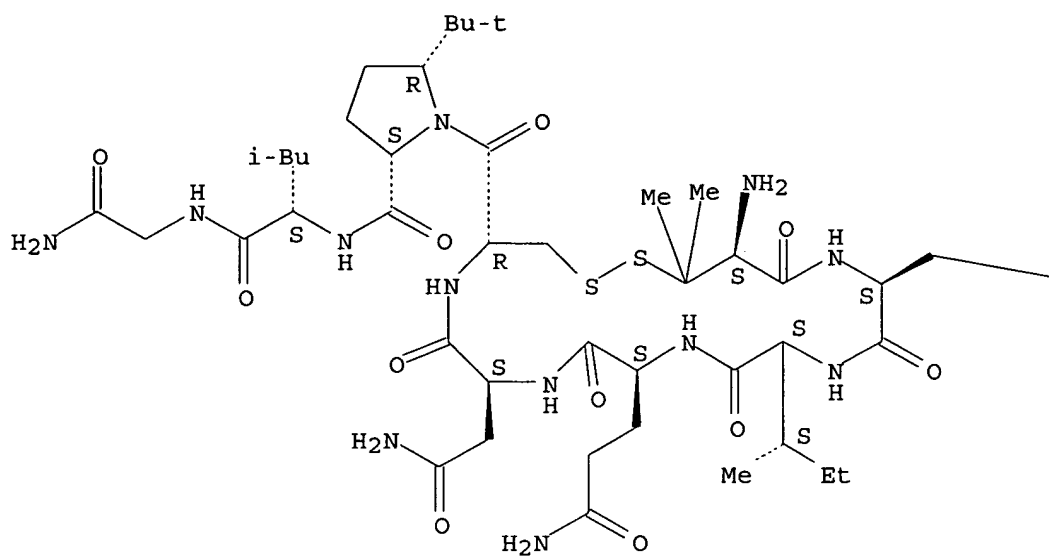


RN 323192-87-6 CAPLUS

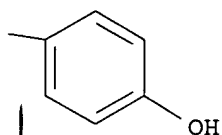
CN Oxytocin, 1-(3-mercapto-D-valine)-7-[(5R)-5-(1,1-dimethylethyl)-L-proline]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT:

6

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 29 OF 44

CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2000:894654 CAPLUS

DOCUMENT NUMBER:

134:237792

TITLE:

The effects of stereochemistry and sequence on 5-*t*-butylproline type VI β -turn mimics

AUTHOR(S):

Halab, Liliane; Lubell, William D.

CORPORATE SOURCE:

Departement de Chimie, Universite de Montreal, Succursale Centre Ville, Montreal, QC, H3C 3J7, Can.

SOURCE:

Peptides for the New Millennium, Proceedings of the American Peptide Symposium, 16th, Minneapolis, MN, United States, June 26-July 1, 1999 (2000), Meeting Date 1999, 305-306. Editor(s): Fields, Gregg B.; Tam, James P.; Barany, George. Kluwer Academic Publishers:

Dordrecht, Neth.

CODEN: 69ATHX

DOCUMENT TYPE:

Conference

LANGUAGE:

English

AB A symposium report. We synthesized N-acetyl-D-Xaa-5-tert-butylproline N'-methanamides Ac-D-Xaa-tBuPro-NHMe (D-Xaa = D-Ala, D-Leu, D-Phe) to examine whether, by favoring the prolyl amide cis-isomer, the bulky 5-tert-Bu substituent could disrupt the type II' geometry and induce a type VI β -turn. As previously observed in the L-series, the steric interactions from the 5-tert-Bu substituent in the Ac-D-Xaa-tBuPro-NHMe series created a predominant prolyl amide cis-isomer population that appeared to adopt a type VIa turn geometry.

IT 224951-42-2 224951-47-7 224951-49-9

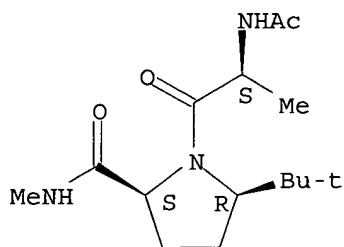
RL: PRP (Properties)

(effects of stereochem. and sequence on tert-butylproline type VI β -turn mimics)

RN 224951-42-2 CAPLUS

CN L-Prolinamide, N-acetyl-L-alanyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-(9CI) (CA INDEX NAME)

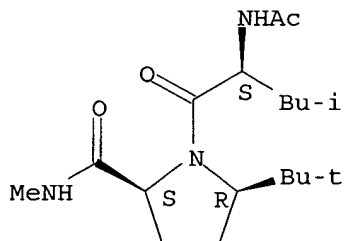
Absolute stereochemistry.



RN 224951-47-7 CAPLUS

CN L-Prolinamide, N-acetyl-L-leucyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-(9CI) (CA INDEX NAME)

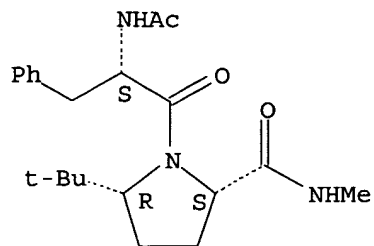
Absolute stereochemistry.



RN 224951-49-9 CAPLUS

CN L-Prolinamide, N-acetyl-L-phenylalanyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



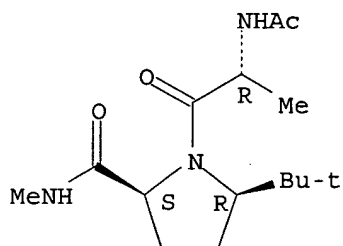
IT 329954-35-0P 329954-38-3P 329954-41-8P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(effects of stereochem. and sequence on tert-butylproline type VI
β-turn mimics)

RN 329954-35-0 CAPLUS

CN L-Prolinamide, N-acetyl-D-alanyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-
(9CI) (CA INDEX NAME)

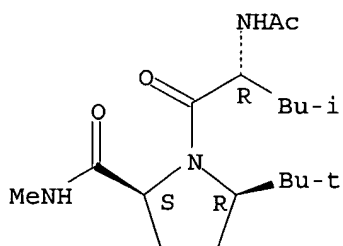
Absolute stereochemistry.



RN 329954-38-3 CAPLUS

CN L-Prolinamide, N-acetyl-D-leucyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-
(9CI) (CA INDEX NAME)

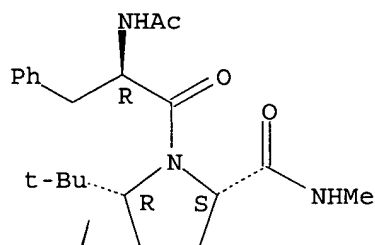
Absolute stereochemistry.



RN 329954-41-8 CAPLUS

CN L-Prolinamide, N-acetyl-D-phenylalanyl-5-(1,1-dimethylethyl)-N-methyl-,
(5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

✓ 151 ANSWER 30 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:742117 CAPLUS

DOCUMENT NUMBER: 133:296665

TITLE: Preparation of amidine- or guanidine-containing peptidomimetics for use as inhibitors of complement proteases

INVENTOR(S): Hillen, Heinz; Schmidt, Martin; Mack, Helmut; Seitz, Werner; Haupt, Andreas; Zechel, Johann-Christian; Kling, Andreas

PATENT ASSIGNEE(S): BASF A.-G., Germany

SOURCE: PCT Int. Appl., 212 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-------------------|------------|
| WO 2000061608 | A2 | 20001019 | WO 2000-EP2710 | 20000328 |
| WO 2000061608 | A3 | 20010111 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2369378 | AA | 20001019 | CA 2000-2369378 | 20000328 |
| EP 1169338 | A2 | 20020109 | EP 2000-920597 | 20000328 |
| EP 1169338 | B1 | 20041103 | | |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | |
| TR 200102913 | T2 | 20020121 | TR 2001-200102913 | 20000328 |
| BR 2000009678 | A | 20020122 | BR 2000-9678 | 20000328 |
| JP 2002542164 | T2 | 20021210 | JP 2000-611550 | 20000328 |
| AT 281466 | E | 20041115 | AT 2000-920597 | 20000328 |
| US 6683055 | B1 | 20040127 | US 2000-539811 | 20000330 |
| ZA 2001007890 | A | 20030929 | ZA 2001-7890 | 20010926 |
| ZA 2001007978 | A | 20030107 | ZA 2001-7978 | 20010928 |
| BG 105978 | A | 20020731 | BG 2001-105978 | 20011004 |
| NO 2001004876 | A | 20011204 | NO 2001-4876 | 20011008 |
| PRIORITY APPLN. INFO.: | | | DE 1999-19915930 | A 19990409 |

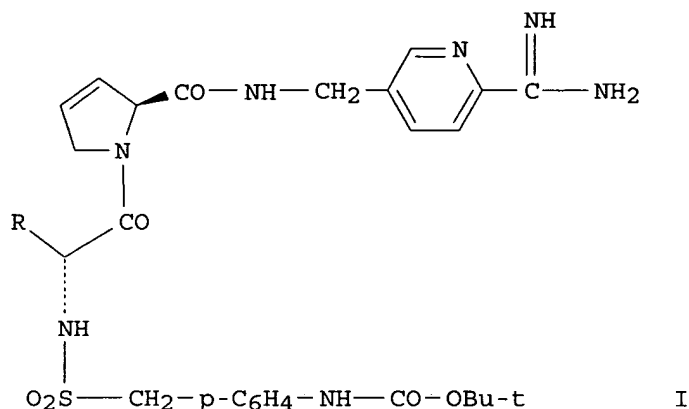
WO 2000-EP2710

W 20000328

OTHER SOURCE(S):

MARPAT 133:296665

GI



AB The invention relates to synthesis of title compds., e.g. [I; R = cyclohexyl(II) or R = cyclohexylmethyl(III)], for use as inhibitors of the complement proteases C1s and C1r in treatment of disease. Compound III was synthesized in seven steps, beginning with (D)-cyclohexylalanine Me ester hydrochloride and 4-nitrobenzylsulfonyl chloride, and including reaction with 3,4-dehydropyrol-1-yl-(3-(6-cyano)picolyl)-amide and conversion of the cyano group to the amidine. In in vivo expts. II had IC₅₀'s for C1s and C1r resp. of 0.6 and 0.9 μmol/l.

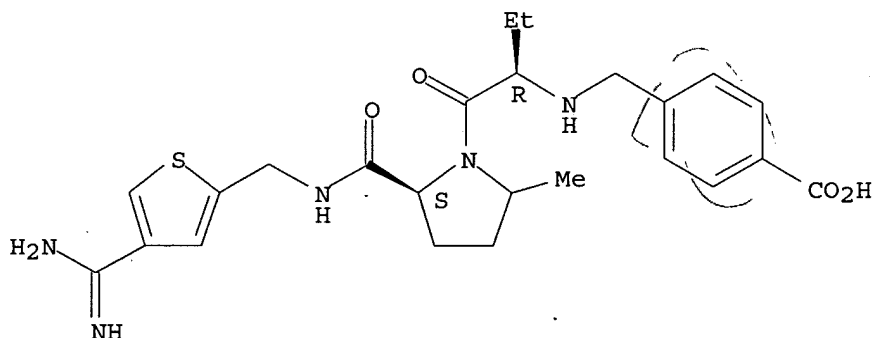
IT 301191-63-9P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amidine- or guanidine-containing peptidomimetics for use as inhibitors of complement proteases)

RN 301191-63-9 CAPLUS

CN Benzoic acid, 4-[[[(1R)-1-[[[(2S)-2-[[[4-(aminoiminomethyl)-2-thienyl]methyl]amino]carbonyl]-5-methyl-1-pyrrolidinyl]carbonyl]propyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 31 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

✓
 ACCESSION NUMBER: 2000:666759 CAPLUS
 DOCUMENT NUMBER: 133:252751
 TITLE: Preparation of substituted proline derivatives and medicinal compositions containing the same
 INVENTOR(S): Shiraishi, Takuya; Haneishi, Tsuyoshi; Haramura, Masayuki
 PATENT ASSIGNEE(S): C & C Research Laboratories, S. Korea
 SOURCE: PCT Int. Appl., 40 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2000055188 | A1 | 20000921 | WO 2000-JP1598 | 20000316 |
| W: | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| KR 2002004971 | A | 20020116 | KR 2001-711826 | 20010917 |
| PRIORITY APPLN. INFO.: | | | JP 1999-70634 | A 19990316 |
| OTHER SOURCE(S): | MARPAT 133:252751 | | | |
| GI | | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Proline derivs. represented by general formula (I; R1 represents formula Q or Q1; wherein A represents CHNH₂, CH[C(:NH)NH₂], or N[C(:NH)NH₂]; X represents N or CH; and Y represents NH₂ or C(:NH)NH₂; R2 represents hydrogen or lower alkyl; R3 represents optionally substituted lower alkyl, optionally substituted aryl or optionally substituted lower alkoxy; R4 represents hydrogen, optionally substituted lower alkyl, optionally substituted lower alkylcarbonyl, optionally substituted lower alkylsufonyl or optionally substituted lower alkoxy carbonyl, R represents hydrogen or lower alkyl; B represents CH₂ or S; and n is an integer of from 1 to 3), stereoisomers thereof or pharmaceutically acceptable salts of the same are prepared. These compds. show an excellent antithrombin activity and thus are useful as drugs such as antithrombotic agents and also available in oral administration and showing little side effect (no data). Thus, trans-4-tert-butoxycarbonylamino-1-aminomethylcyclohexane was condensed with (S)-N-[(2R,3S)-N-benzyloxycarbonyl-3-phenylpropyl]proline using HOBt and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in DMF under stirring for 1 day followed by hydrogenolysis over 5% Pd/C in AcOH/EtOH to give trans-4-tert-butoxycarbonylamino-1-[(S)-N-[(2R,3S)-3-phenylpropyl]propyl]aminomethylcyclohexane. The latter compound was alkylated by Et 4-bromobutyrate in the presence of diisopropylethylamine in MeCN at 65° for 3 h followed by treatment with CF₃CO₂H and then with a mixture of 2 N aqueous NaOH and EtOH to give a dipeptide derivative, namely

trans-4-amino-1-[(S)-N-[(2R,3S)-N'-(3-carboxypropyl)-3-phenylpropyl]propyl]aminomethylcyclohexane (II).

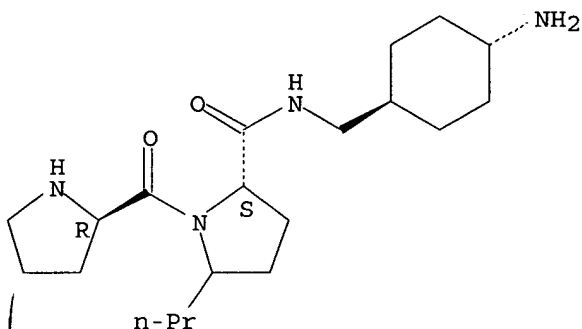
IT 294627-10-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted proline derivs. with antithrombin activity as antithrombotic agents)

RN 294627-10-4 CAPLUS

CN L-Prolinamide, D-prolyl-N-[(trans-4-aminocyclohexyl)methyl]-5-propyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 32 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:188651 CAPLUS

DOCUMENT NUMBER: 133:12851

TITLE: A Study of the Relationship between Biological Activity and Prolyl Amide Isomer Geometry in Oxytocin Using 5-tert-Butylproline To Augment the Cys6-Pro7 Amide Cis-Isomer Population

AUTHOR(S): Belec, Laurent; Slaninova, Jirina; Lubell, William D.

CORPORATE SOURCE: Departement de chimie, Universite de Montreal, Montreal, QC, H3C 3J7, Can.

SOURCE: Journal of Medicinal Chemistry (2000), 43(8), 1448-1455

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Three [5-t-BuPro7]oxytocin analogs were synthesized by substituting (2S,5R)-5-tert-butylproline for proline in oxytocin, [Mpa1]oxytocin, and [dPen1]oxytocin. Relative to oxytocin, [5-t-BuPro7]oxytocin and [Mpa1,5-t-BuPro7]oxytocin exhibited strongly reduced binding affinity to the receptor; however, both peptides maintained the pharmacophore characteristics responsible for signal transfer evoking the same maximal response as oxytocin in the single-dose procedure and exhibiting partial agonistic activity in the cumulative dose-response procedure. Although [dPen1]oxytocin exhibited inhibitory as well as partial agonistic activity, [dPen1,5-t-BuPro7]oxytocin exhibited only inhibitory potency with a similar in vitro pA2 value of 7.50 in the absence of magnesium. In the presence of magnesium, [dPen1,5-t-BuPro7]oxytocin exhibited stronger

inhibitory potency than [dPen1]oxytocin and no partial agonism. Assignment of the proton signals for the 5-tert-butylprolyl amide cis- and trans-isomers by two-dimensional NMR expts. in water indicated that the Cys6-Pro7 peptide bond cis-isomer population was augmented relative to the prolyl peptides and measured resp. at 35%, 33%, and 20% in the 5-tert-butylproline7 analogs of oxytocin, [Mpa1]oxytocin and [dPen1]oxytocin. Although caution must be taken when relating the increase in cis-isomer population with an influence on biol. activity in [5-t-BuPro7]oxytocin analogs, the synthesis and evaluation of analogs 1-3 have provided addnl. evidence that can be used to support the hypothesis that the prolyl amide cis-isomer may favor antagonism and the trans-isomer is necessary for agonist activity.

IT 268219-94-9P 268219-95-0P 268219-96-1P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)

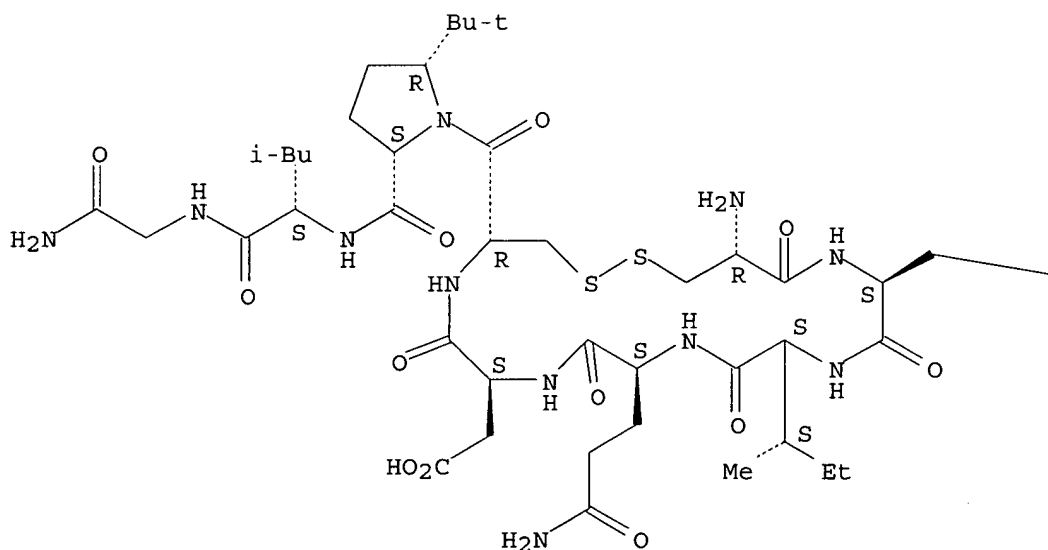
(relationship between biol. activity and prolyl amide isomer geometry in oxytocin using 5-tert-butylproline to augment Cys6-Pro7 amide cis-isomer population)

RN 268219-94-9 CAPLUS

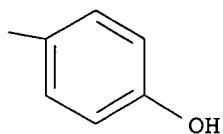
CN Glycinamide, L-cysteinyl-L-tyrosyl-L-isoleucyl-L-glutaminyl-L- α -aspartyl-L-cysteinyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-L-leucyl-, cyclic (1 \rightarrow 6)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

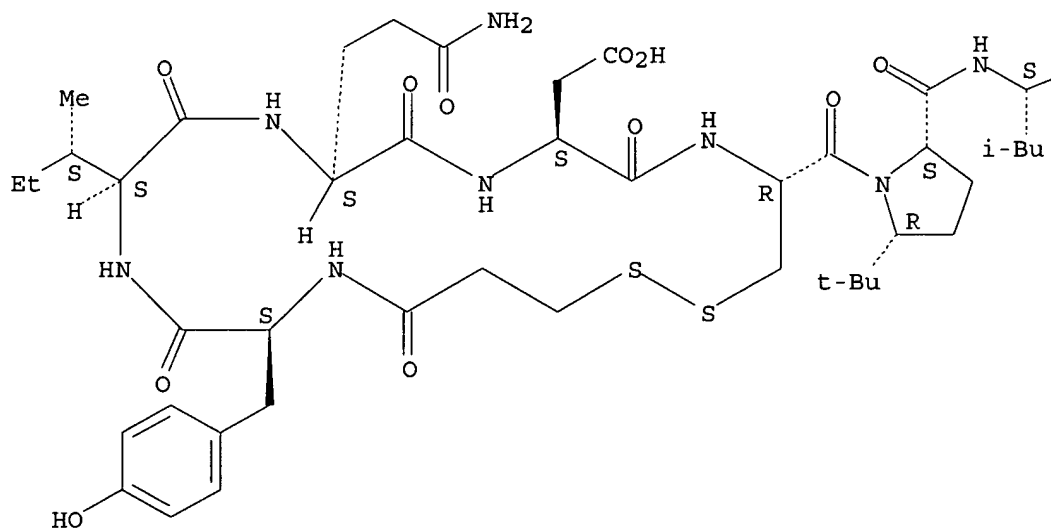


RN 268219-95-0 CAPLUS

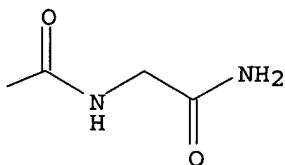
CN Glycinamide, N-(3-mercapto-1-oxopropyl)-L-tyrosyl-L-isoleucyl-L-glutaminyl-L- α -aspartyl-L-cysteinyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-L-leucyl-, cyclic (1 \rightarrow 5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



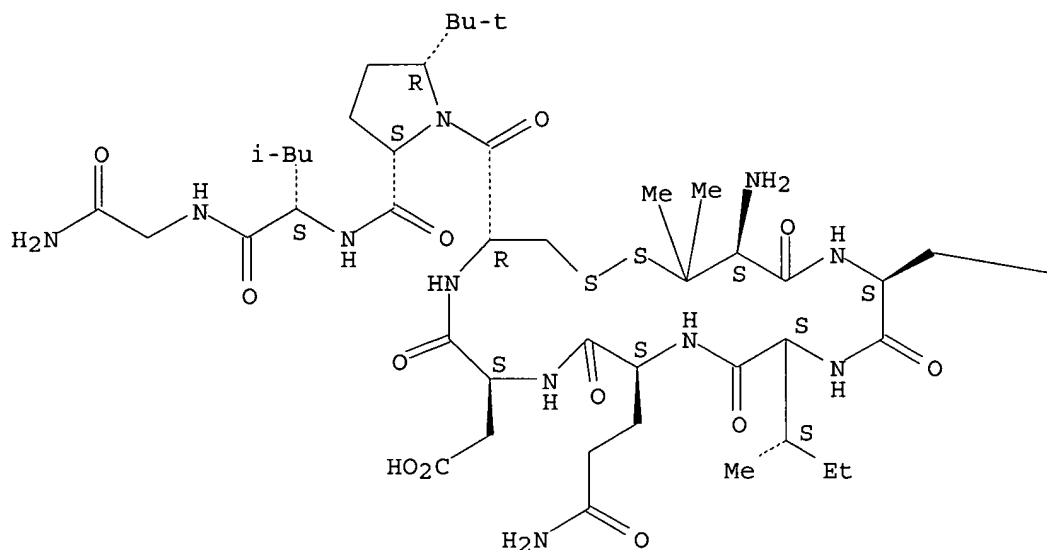
PAGE 1-B



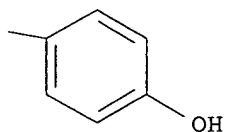
RN 268219-96-1 CAPLUS
 CN Glycinamide, 3-mercapto-D-valyl-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-
 α -aspartyl-L-cysteinyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-L-leucyl-
 , cyclic (1 \rightarrow 6)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

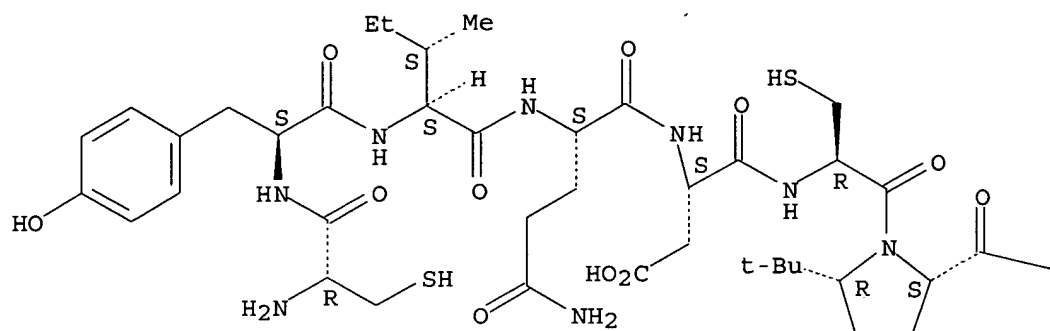


IT **268220-00-4P 268220-01-5P 268220-02-6P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (relationship between biol. activity and prolyl amide isomer geometry
 in oxytocin using 5-tert-butylproline to augment Cys6-Pro7 amide
 cis-isomer population)
 RN 268220-00-4 CAPLUS
 CN Glycinamide, L-cysteinyl-L-tyrosyl-L-isoleucyl-L-glutaminyl-L- α -
 aspartyl-L-cysteinyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-L-leucyl- (9CI)

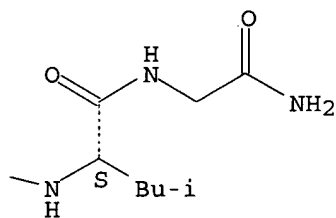
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

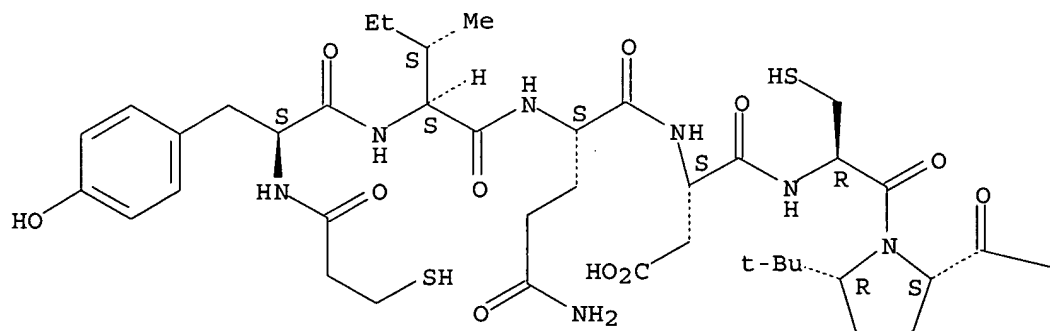


RN 268220-01-5 CAPLUS

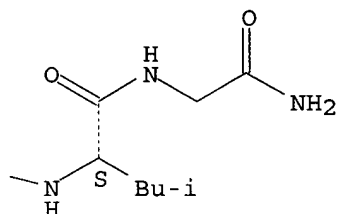
CN Glycinamide, N-(3-mercapto-1-oxopropyl)-L-tyrosyl-L-isoleucyl-L-glutaminyl-L- α -aspartyl-L-cysteinyl-(5R)-5-(1,1-dimethylethyl)-L-prolyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

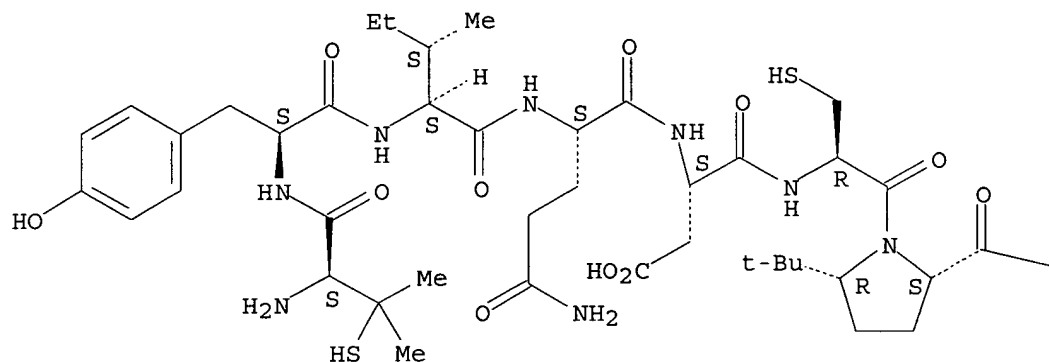


RN 268220-02-6 CAPLUS

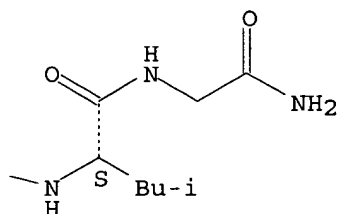
CN Glycinamide, 3-mercapto-D-valyl-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-
α-aspartyl-L-cysteinyl- (5R) -5- (1,1-dimethylethyl) -L-prolyl-L-leucyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



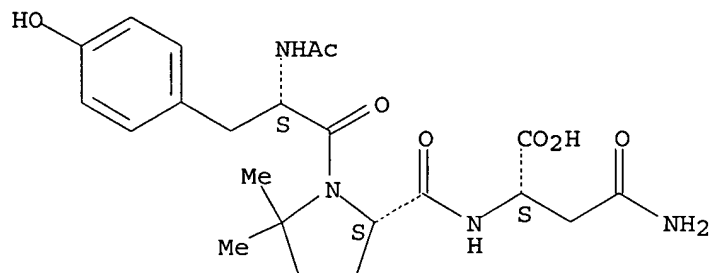
REFERENCE COUNT:

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THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

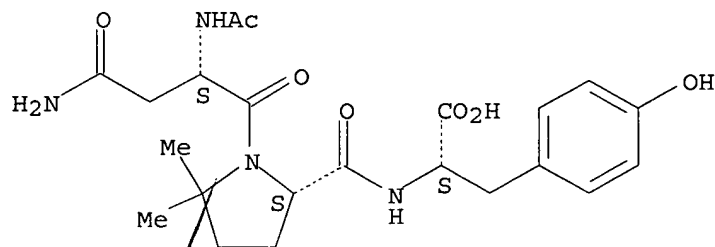
L51 ANSWER 33 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:771160 CAPLUS
DOCUMENT NUMBER: 132:119203
TITLE: Retention of the Cis Proline Conformation in
Tripeptide Fragments of Bovine Pancreatic Ribonuclease
A Containing a Non-natural Proline Analogue,
5,5-Dimethylproline
AUTHOR(S): An, Seong Soo A.; Lester, Cathy C.; Peng, Jin-Lin; Li,
Yue-Jin; Rothwarf, David M.; Welker, Ervin;
Thannhauser, Theodore W.; Zhang, L. S.; Tam, James P.;
Scheraga, Harold A.
CORPORATE SOURCE: Baker Laboratory of Chemistry and Chemical Biology,
Cornell University, Ithaca, NY, 14853-1301, USA
SOURCE: Journal of the American Chemical Society (1999),
121(49), 11558-11566
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Attention is focused on L-5,5-dimethylproline (dmP) as a substitute to
lock L-proline (Pro) in a cis conformation in peptides and proteins, to
prevent cis/trans isomerization when a protein with cis X-Pro peptide
groups unfolds. Procedures have been developed to obtain optically pure
L-dmP and to incorporate this sterically hindered residue as the central
one in tripeptides that are suitable for fragment coupling to prepare
synthetic proteins. Based on the sequences of residues 92-94
(Tyr-Pro-Asn:YPN) and 113-115 (Asn-Pro-Tyr: NPY) in bovine pancreatic
RNase A, in which the X-Pro peptide groups are in the cis conformation,
the tripeptides Ac-Tyr-dmP-Asn (YdmPN) and Ac-Asn-dmP-Tyr (NdmPY) were
synthesized, and their structures were determined by 2D 1H NMR spectroscopy.
YdmPN was found to exist solely in the cis conformation between 6 and
60°, whereas NdmPY was found to have some trans component that
increased from about 10% to about 21% as the temperature increased over the
range between 6 and 80°. Both YdmPN and cis-NdmPY adopt a type VI
reverse turn, as does proline. The NMR structures of YdmPN and cis-NdmPY
are comparable with the x-ray structures of the corresponding portions of
RNase A, and the NMR structure of trans-NdmPY is compatible with the x-ray
structure of the isolated tripeptide, Ac-NPY. These results demonstrate
that L-dmP is a promising substitute for proline in a variety of protein
problems to constrain the X-Pro peptide group to the cis conformation.
IT 256240-41-2P 256240-42-3P
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic
preparation); BIOL (Biological study); PREP (Preparation)
(retention of cis proline conformation in tripeptide fragments of
bovine pancreatic RNase A containing non-natural proline analog,
5,5-dimethylproline)
RN 256240-41-2 CAPLUS
CN L-Asparagine, N-acetyl-L-tyrosyl-5,5-dimethyl-L-prolyl- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.



RN 256240-42-3 CAPLUS
 CN L-Tyrosine, N2-acetyl-L-asparaginyl-5,5-dimethyl-L-prolyl- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 34 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:613942 CAPLUS

DOCUMENT NUMBER: 131:243593

TITLE: Preparation of peptides as inhibitors of caspases

INVENTOR(S): Wannamaker, Marion W.; Bemis, Guy W.; Charifson, Paul
 S.; Lauffer, David J.; Mullican, Michael D.; Murcko,
 Mark A.; Wilson, Keith P.; Janetka, James W.; Davies,
 Robert J.; Grillot, Anne-Laure; Shi, Zhan; Forster,
 Cornelia J.

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 297 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|--|----------|-----------------|----------|
| WO 9947545 | A2 | 19990923 | WO 1999-US5919 | 19990319 |
| WO 9947545 | A3 | 19991125 | | |
| W: | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW | | | |
| RW: | GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, | | | |

ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
 CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|--|----|----------|-------------------|-------------|
| CA 2324226 | AA | 19990923 | CA 1999-2324226 | 19990319 |
| AU 9930986 | A1 | 19991011 | AU 1999-30986 | 19990319 |
| AU 769033 | B2 | 20040115 | | |
| BR 9909660 | A | 20001121 | BR 1999-9660 | 19990319 |
| EP 1064298 | A2 | 20010103 | EP 1999-912662 | 19990319 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002506878 | T2 | 20020305 | JP 2000-536738 | 19990319 |
| TR 200103406 | T2 | 20020621 | TR 2001-200103406 | 19990319 |
| NZ 506963 | A | 20031031 | NZ 1999-506963 | 19990319 |
| NZ 528282 | A | 20050527 | NZ 1999-528282 | 19990319 |
| RU 2274642 | C2 | 20060420 | RU 2000-126298 | 19990319 |
| ZA 2000004652 | A | 20020205 | ZA 2000-4652 | 20000905 |
| NO 2000004546 | A | 20001109 | NO 2000-4546 | 20000912 |
| US 6531474 | B1 | 20030311 | US 2000-665503 | 20000919 |
| BG 104863 | A | 20010430 | BG 2000-104863 | 20001016 |
| US 2003232986 | A1 | 20031218 | US 2002-314103 | 20021206 |
| AU 2003255217 | A1 | 20031113 | AU 2003-255217 | 20031022 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 1998-78770P | A1 19980319 |
| | | | AU 1999-30986 | A3 19990319 |
| | | | WO 1999-US5919 | W 19990319 |
| | | | US 2000-665503 | A3 20000919 |

OTHER SOURCE(S): MARPAT 131:243593

AB Peptides R1NR2XCONR4CR52CONHY [Y = CH(CHO)CH2(CH2)mCOR7, (m = 0 or 1 and R7 = OH or ester, NHOH) or cyclic lactol derivative when R7 is OH; X = CR32 or NR3 (R3 = H, an amino acid side chain, alkyl, cycloalkyl, aryl, etc.); R1 = H, R8, COR8, COCOR8, SO2R8, SOR8, CO2R8, CONHR8, SO2NHR8, SONHR8, COCONHR8, COCH:CHR8, etc. (R8 = alkyl, cycloalkyl, aryl, etc.); R2 = H or R2 and R3 may form a ring; R4 = H and R5 = H, amino acid side chain, R8, etc. or R4 and R5 may form a ring] were prepared as inhibitors of caspases. Thus, p-AcNHC6H4CO-L-Val-L-Pro-NHCH(CHO)CH2CO2H-(S) was prepared by the solid-phase method and showed $k_i < 10$ nm for inhibition of interleukin-1 β converting enzyme (ICE, caspase-1).

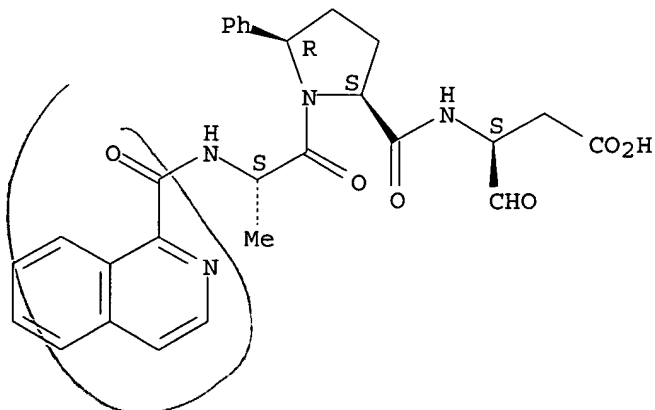
IT 244132-33-0P 244132-56-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of peptides as inhibitors of caspases)

RN 244132-33-0 CAPLUS

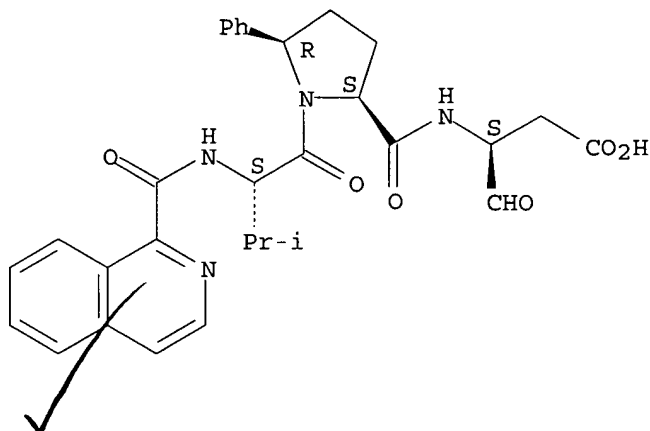
CN L-Prolinamide, N-(1-isoquinolinylcarbonyl)-L-alanyl-N-[(1S)-2-carboxy-1-formylethyl]-5-phenyl-, (5R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 244132-56-7 CAPLUS
 CN L-Prolinamide, N-(1-isoquinolinylcarbonyl)-L-valyl-N-[(1S)-2-carboxy-1-formylethyl]-5-phenyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 35 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:396590 CAPLUS

DOCUMENT NUMBER: 131:225454

TITLE: Retention of a cis-proline rotamer in a small fragment of RNase A containing a non-natural proline analog - an NMR study

AUTHOR(S): Li, Yue-Jin; Lester, Cathy C.; Rothwarf, David M.; Peng, Jin-Lin; Thannhauser, Theodore W.; Zhang, Lianshan; Tam, James P.; Scheraga, Harold A.

CORPORATE SOURCE: Baker Laboratory of Chemistry, Cornell University, Ithaca, NY, 14853-1301, USA

SOURCE: Peptides: Frontiers of Peptide Science, Proceedings of the American Peptide Symposium, 15th, Nashville, June 14-19, 1997 (1999), Meeting Date 1997, 422-423.

Editor(s): Tam, James P.; Kaumaya, Pravin T. P.

Kluwer: Dordrecht, Neth.

CODEN: 67UCAR

DOCUMENT TYPE: Conference

LANGUAGE: English

AB In this study, an analog tripeptide corresponding to the sequence Tyr92-Pro93-Asn94 of RNase A was synthesized with proline replaced by a non-natural amino acid, 5,5-dimethylproline. The bulky Me groups were introduced to retard the proline isomerization process. NMR was used to characterize the solution conformation of the peptide.

IT 244097-58-3

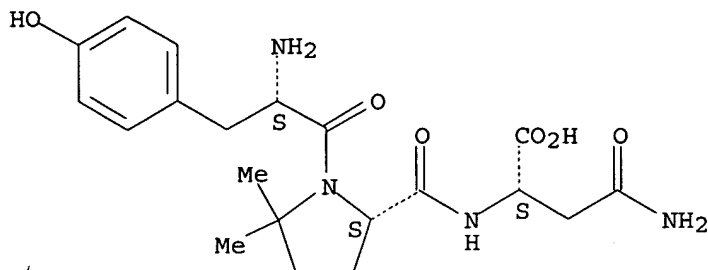
RL: PRP (Properties)

(retention of cis-proline rotamer in a small fragment of RNase A containing a non-natural proline analog)

RN 244097-58-3 CAPLUS

CN L-Asparagine, L-tyrosyl-5,5-dimethyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 36 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:222746 CAPLUS

DOCUMENT NUMBER: 130:352530

TITLE: Use of Steric Interactions To Control Peptide Turn Geometry. Synthesis of Type VI β -Turn Mimics with 5-tert-Butylproline

AUTHOR(S): Halab, Liliane; Lubell, William D.

CORPORATE SOURCE: Departement de chimie, Universite de Montreal, Montreal, QC, H3C 3J7, Can.

SOURCE: Journal of Organic Chemistry (1999), 64(9), 3312-3321
CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In order to develop a method for generating type VIa β -turn mimics, the influence of steric interactions on peptide geometry was studied. The studied peptides were Ac-Ala-Pro-NHMe, Ac-Leu-Pro-NHMe and Ac-Xaa-tBuPro-NHMe [Xaa = Ala, Met, Leu, Val, Phe; tBuPro = (2S,5R)-5-tert-butylproline]. The relative populations of prolyl cis- and trans-amide isomers in the above dipeptides were measured in CHCl₃, DMSO, and in water by ¹H NMR spectroscopy. Although the peptide bond in Ala-Pro dipeptides favored the trans-amide isomer, the peptide bond in Xaa-tBuPro dipeptides favored the cis-amide isomer. Measurements of the influence of solvent and temperature on the chemical shift values for the amide proton signals

of the cis-amide conformer of Xaa-tBuPro indicated that the N'-methanamide was engaged in a hydrogen bond with the acetamide carbonyl in a type VIa β -turn conformation. Anal. of Ac-Leu-tBuPro-NHMe in the solid state by x-ray diffraction showed the cis-amide conformer which adopted a geometry characteristic of the central, i + 1 and i + 2 residues of an ideal type VIa β -turn. In contrast to Ac-Ala-Pro-NHMe and Ac-Leu-Pro-NHMe (the unsubstituted prolyl peptides), Ac-Ala-tBuPro-NHMe and Ac-Leu-tBuPro-NHMe maintained ordered β -turn conformations in solution that were shown to be independent of solvent composition by a comparison

of their CD spectra obtained in water and MeCN. The NMR, x-ray, and CD data all confirm that the steric interactions of the 5-tert-butylproline residue induced the dipeptides containing it to adopt a type VIa β -turn conformation.

IT 224951-42-2P 224951-45-5P 224951-47-7P

224951-48-8P 224951-49-9P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)

(preparation and conformational analyses of dipeptides containing proline

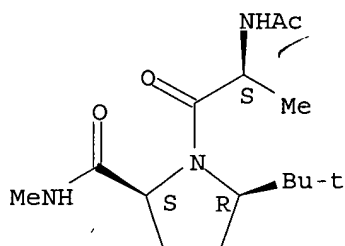
and

5-tert-butylproline to study peptide turn geometry)

RN 224951-42-2 CAPLUS

CN L-Prolinamide, N-acetyl-L-alanyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-
(9CI) (CA INDEX NAME)

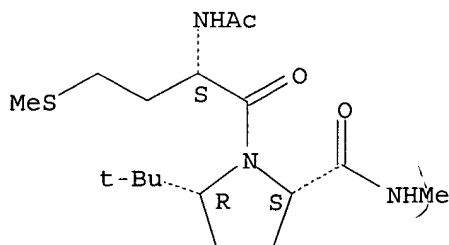
Absolute stereochemistry.



RN 224951-45-5 CAPLUS

CN L-Prolinamide, N-acetyl-L-methionyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-
(9CI) (CA INDEX NAME)

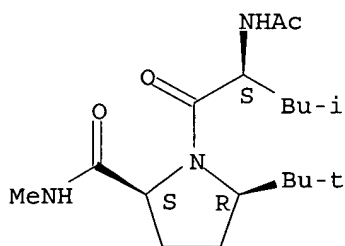
Absolute stereochemistry.



RN 224951-47-7 CAPLUS

CN L-Prolinamide, N-acetyl-L-leucyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-
(9CI) (CA INDEX NAME)

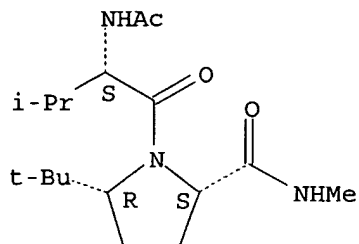
Absolute stereochemistry.



RN 224951-48-8 CAPLUS

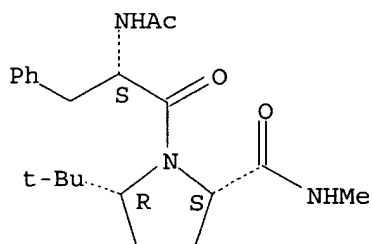
CN L-Prolinamide, N-acetyl-L-valyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 224951-49-9 CAPLUS
 CN L-Prolinamide, N-acetyl-L-phenylalanyl-5-(1,1-dimethylethyl)-N-methyl-,
 (5R)- (9CI) (CA INDEX NAME)

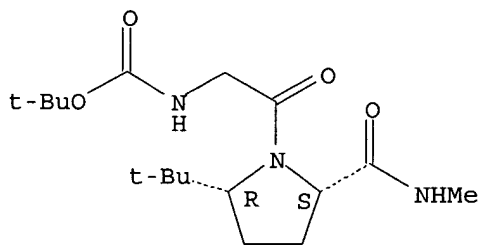
Absolute stereochemistry.



IT 224951-67-1P 224951-68-2P 224951-69-3P
 224951-70-6P 224951-71-7P 224951-72-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT.
 (Reactant or reagent)
 (preparation and conformational analyses of dipeptides containing proline
 and 5-tert-butylproline to study peptide turn geometry)

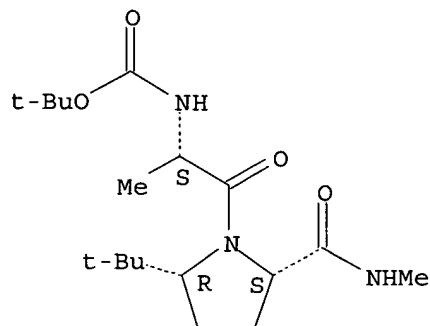
RN 224951-67-1 CAPLUS
 CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]glycyl-5-(1,1-
 dimethylethyl)-N-methyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 224951-68-2 CAPLUS
 CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-alanyl-5-(1,1-
 dimethylethyl)-N-methyl-, (5R)- (9CI) (CA INDEX NAME)

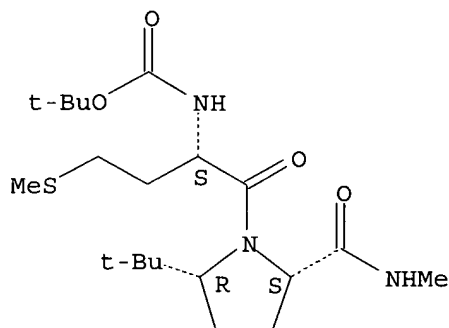
Absolute stereochemistry.



RN 224951-69-3 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-methionyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)- (9CI) (CA INDEX NAME)

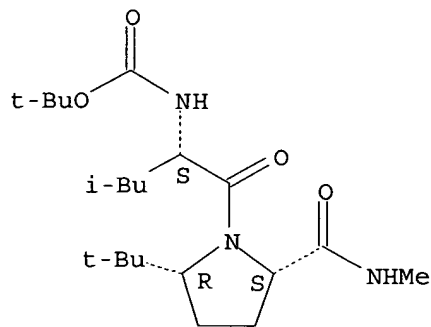
Absolute stereochemistry.



RN 224951-70-6 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)- (9CI) (CA INDEX NAME)

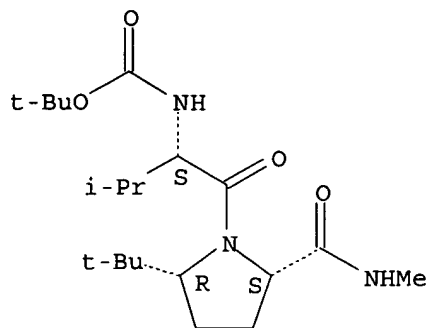
Absolute stereochemistry.



RN 224951-71-7 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-valyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)- (9CI) (CA INDEX NAME)

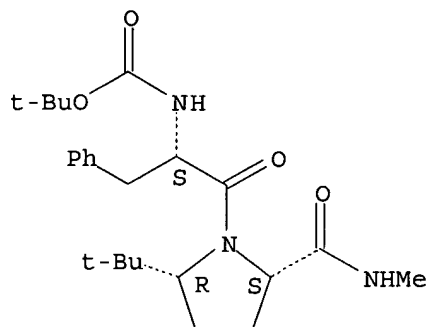
Absolute stereochemistry.



RN 224951-72-8 CAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 224951-39-7P

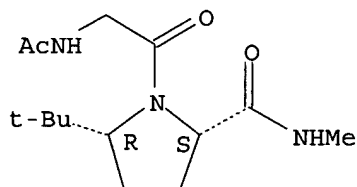
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and conformational analyses of dipeptides containing proline and 5-tert-butylproline to study peptide turn geometry)

RN 224951-39-7 CAPLUS

CN L-Prolinamide, N-acetylglycyl-5-(1,1-dimethylethyl)-N-methyl-, (5R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

108

THERE ARE 108 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L51 ANSWER 37 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1999:126924 CAPLUS
 DOCUMENT NUMBER: 130:168665
 TITLE: Preparation of hepatitis C inhibitory peptides
 INVENTOR(S): Llinas-Brunet, Montse; Poupart, Marc-Andre; Rancourt, Jean; Simoneau, Bruno; Tsantrizos, Youla; Wernic, Dominik
 PATENT ASSIGNEE(S): Boehringer Ingelheim (Canada) Ltd., Can.
 SOURCE: PCT Int. Appl., 158 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| WO 9907733 | A2 | 19990218 | WO 1998-CA765 | 19980810 |
| WO 9907733 | A3 | 19990520 | | |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2294049 | AA | 19990218 | CA 1998-2294049 | 19980810 |
| AU 9887956 | A1 | 19990301 | AU 1998-87956 | 19980810 |
| AU 757783 | B2 | 20030306 | | |
| EP 1003775 | A2 | 20000531 | EP 1998-939450 | 19980810 |
| EP 1003775 | B1 | 20050316 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2001512743 | T2 | 20010828 | JP 2000-506235 | 19980810 |
| NZ 503262 | A | 20021025 | NZ 1998-503262 | 19980810 |
| AT 291032 | E | 20050415 | AT 1998-939450 | 19980810 |
| PT 1003775 | T | 20050729 | PT 1998-939450 | 19980810 |
| ES 2241157 | T3 | 20051016 | ES 1998-939450 | 19980810 |
| US 6767991 | B1 | 20040727 | US 1999-368670 | 19990805 |
| MX 200001498 | A | 20001110 | MX 2000-1498 | 20000211 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 1997-55186P | P 19970811 |
| | | | US 1998-131758 | B2 19980810 |
| | | | US 1998-95945P | P 19980810 |
| | | | WO 1998-CA765 | W 19980810 |
| | | | US 1998-219939 | B1 19981223 |

OTHER SOURCE(S): MARPAT 130:168665

AB Peptides B[NHCHR6CO]a[NHCHR5CO]bQCHR4C(:Z)NHCHR3COWNHCR1R1'COA (when Q is CH2 and a and b are 0, B is an amide derivative or when Q is NH or alkylimino and a and b are 0 or 1, B is an acyl derivative; R6 = carboxyalkyl; R5 = alkyl or carboxyalkyl; R4 = alkyl, cycloalkyl, alkylcycloalkyl; Z = oxo or thioxo; R3 = alkyl, carboxyalkyl, cycloalkyl, alkylcycloalkyl; W is an amino acid residue such as proline; R1' = H and R1 = alkyl, mercapto- or haloalkyl or R1' and R1 together form a 3- to 6-membered ring; A is hydroxy or a pharmaceutically acceptable salt or ester) were prepared as hepatitis C virus inhibitors. Thus, Ac-Asp-D-Glu-Chg-Val-X-Nva-OH [Chg = cyclohexylglycine, X = 4(R)-(2-naphthylmethoxy)proline, and Nva = norvaline residue], prepared by step-wise couplings in solution, showed IC50 = 0.028 µM in the NS3 protease/NS4A cofactor peptide radiometric assay.

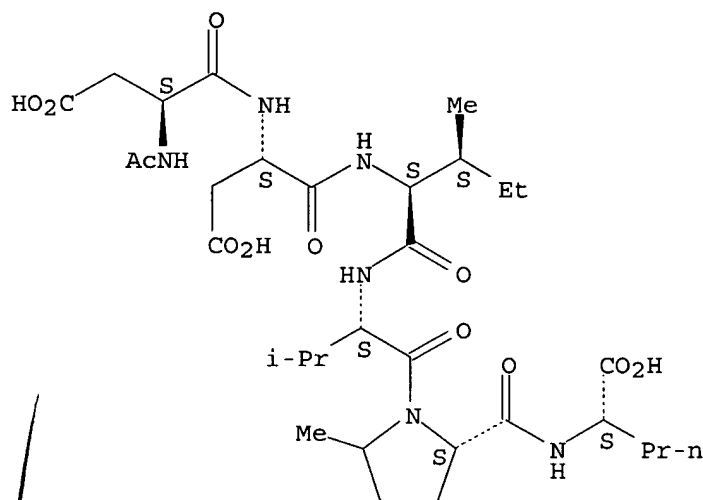
IT 220426-35-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of hepatitis C inhibitory peptides)

RN 220426-35-7 CAPLUS

CN L-Norvaline, N-acetyl-L- α -aspartyl-L- α -aspartyl-L-isoleucyl-L-valyl-5-methyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 38 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:597958 CAPLUS

DOCUMENT NUMBER: 129:339947

TITLE: Increasing the cis peptide bond conformation between Tyr1 and Pro2 in β -casomorphin-5: implications on the receptor affinity

AUTHOR(S): Van Betsbrugge, Jo; Verheyden, Patricia; Tourwe, Dirk
CORPORATE SOURCE: Laboratorium voor Organische Chemie, Vrije Universiteit Brussel, Brussels, B-1050, Belg.

SOURCE: Peptides 1996, Proceedings of the European Peptide Symposium, 24th, Edinburgh, Sept. 8-13, 1996 (1998), Meeting Date 1996, 859-860. Editor(s): Ramage, Robert; Epton, Roger. Mayflower Scientific: Kingswinford, UK.
CODEN: 66RCA5

DOCUMENT TYPE: Conference

LANGUAGE: English

AB Models for the bioactive conformation of β -casomorphin-5 have been proposed in which a cis peptide bond occurs between the residues Tyr1 and Pro2. The authors undertook a study to evaluate the validity of the proposed model by introduction of cis-5-methylproline and trans-5-methylproline in β -casomorphin-5. The results do not confirm the proposed bioactive model containing a cis Tyr1-Pro2 peptide bond, as substitution at the 2- or 5-position of Pro2 strongly reduced receptor affinity.

IT 160033-54-5 215531-38-7

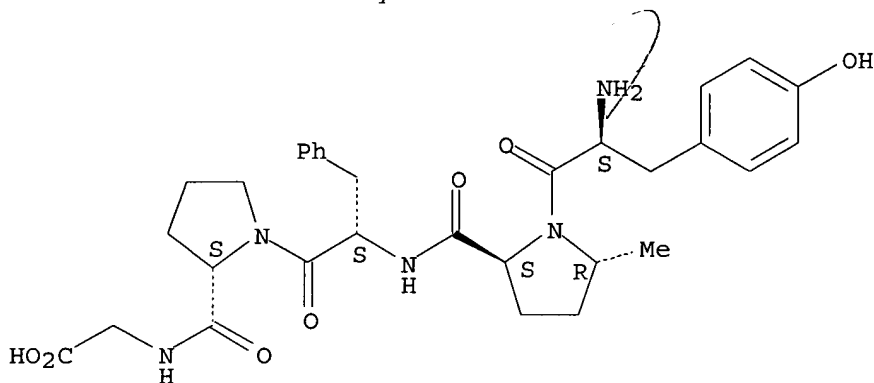
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP

(Properties); BIOL (Biological study); PROC (Process)
 (increasing cis peptide bond conformation between Tyr1 and Pro2 in
 β -casomorphin-5 and implications on receptor affinity)

RN 160033-54-5 CAPLUS

CN Glycine, N-[1-[N-(trans-5-methyl-1-L-tyrosyl-L-prolyl)-L-phenylalanyl]-L-prolyl]- (9CI) (CA INDEX NAME)

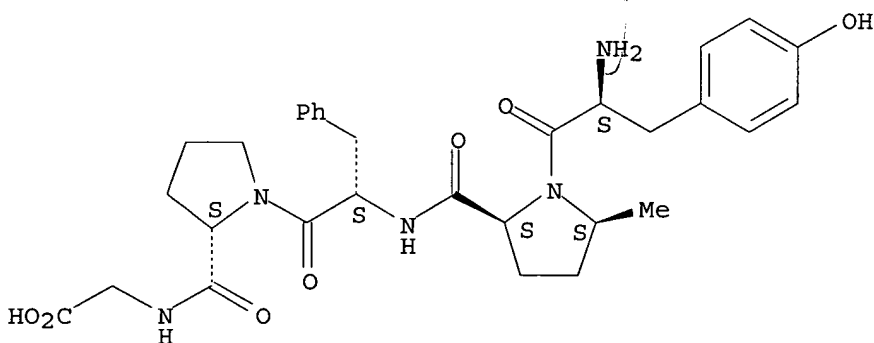
Absolute stereochemistry.



RN 215531-38-7 CAPLUS

CN Glycine, L-tyrosyl-(5S)-5-methyl-L-prolyl-L-phenylalanyl-L-prolyl- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

6

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ✓ ANSWER 39 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:772197 CAPLUS

DOCUMENT NUMBER: 128:34687

TITLE: Preparation of substituted heterocyclic thrombin
 inhibitors

INVENTOR(S): Das, Jagabandhu; Kimball, Spencer D.; Lau, Wan Fang

PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA

SOURCE: U.S., 21 pp., Cont. of U. S. Ser. No. 215,433,
 abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

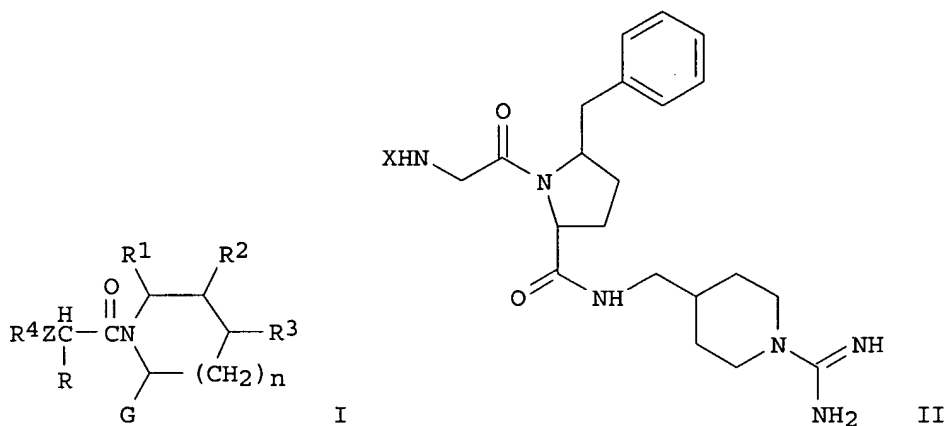
English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--------|-----------|-----------------|-------------|
| US 5691356 | A | 19971125 | US 1996-708292 | 19960904 |
| PRIORITY APPLN. INFO.: | | | US 1994-215433 | B1 19940321 |
| OTHER SOURCE(S): | MARPAT | 128:34687 | | |

GI



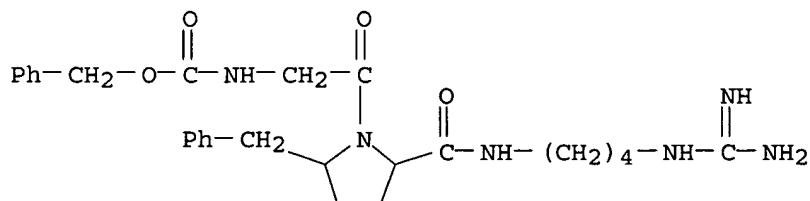
AB The title compds. (I; Z = NR₅, O; G = amido moiety which includes a cyclic member; R = OH, hydroxyalkyl, aminoalkyl, etc.; R₁ = lower alkyl, cycloalkyl, aryl, etc.; R₂, R₃ = H, lower alkyl, cycloalkyl, aryl, aralkyl, OH, etc.; R₄ = H, lower alkyl, aralkyl, aryl, etc.; R₅ = H, lower alkyl, aryl, aralkyl; n = 0-2) are prepared I are useful as thrombin inhibitors (no data). Thus, compound (II; X = H).CF₃CO₂H was treated with Et₃N and then reacted with MeSO₂Cl to give 51% the title compound II (X = MeSO₂).

IT 199611-85-3P 199611-86-4P 199611-87-5P
199611-88-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted heterocyclic thrombin inhibitors)

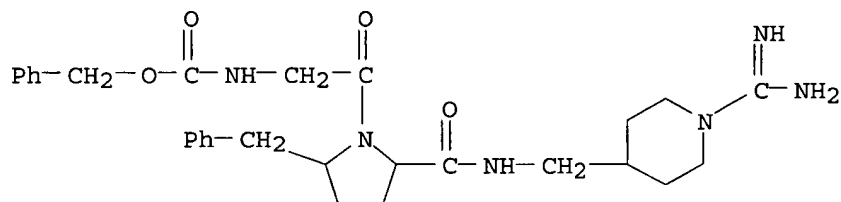
RN 199611-85-3 CAPLUS

CN Prolinamide, N-[(phenylmethoxy)carbonyl]glycyl-N-[4-[(aminoiminomethyl)amino]butyl]-5-(phenylmethyl)- (9CI) (CA INDEX NAME)



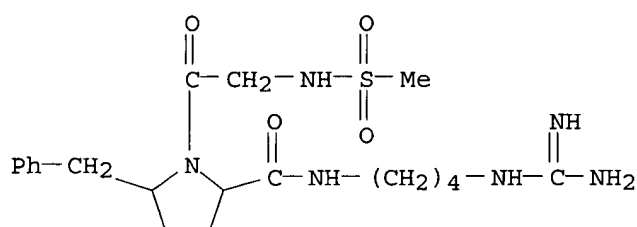
RN 199611-86-4 CAPLUS

CN Prolinamide, N-[(phenylmethoxy)carbonyl]glycyl-N-[[1-(aminoiminomethyl)-4-piperidiny]methyl]-5-(phenylmethyl)- (9CI) (CA INDEX NAME)



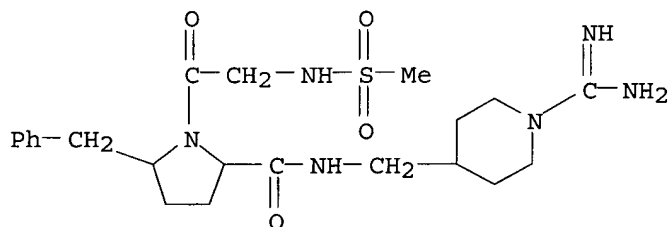
RN 199611-87-5 CAPLUS

CN Prolinamide, N-(methylsulfonyl)glycyl-N-[4-[(aminoiminomethyl)amino]butyl]-5-(phenylmethyl)- (9CI) (CA INDEX NAME)



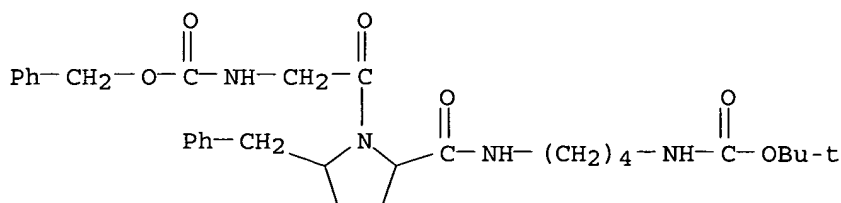
RN 199611-88-6 CAPLUS

CN Prolinamide, N-(methylsulfonyl)glycyl-N-[[1-(aminoiminomethyl)-4-piperidinyl]methyl]-5-(phenylmethyl)- (9CI) (CA INDEX NAME)

IT 199611-96-6P 199611-97-7P 199611-98-8P
199611-99-9PRL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted heterocyclic thrombin inhibitors)

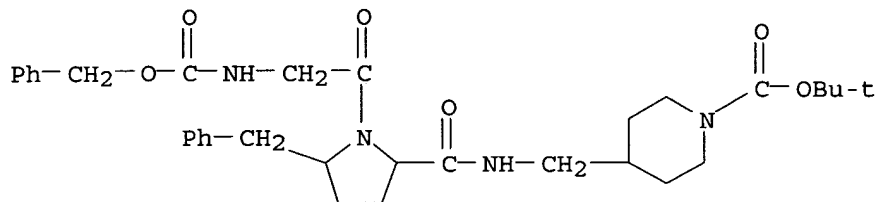
RN 199611-96-6 CAPLUS

CN Prolinamide, N-[(phenylmethoxy)carbonyl]glycyl-N-[4-[(1,1-dimethylethoxy)carbonyl]amino]butyl]-5-(phenylmethyl)- (9CI) (CA INDEX NAME)



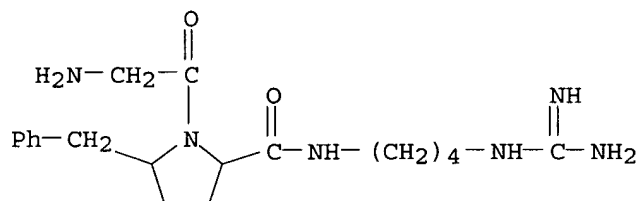
RN 199611-97-7 CAPLUS

CN Prolinamide, N-[(phenylmethoxy)carbonyl]glycyl-N-[[1-[(1,1-dimethylethoxy)carbonyl]-4-piperidinyl]methyl]-5-(phenylmethyl)- (9CI)
(CA INDEX NAME)



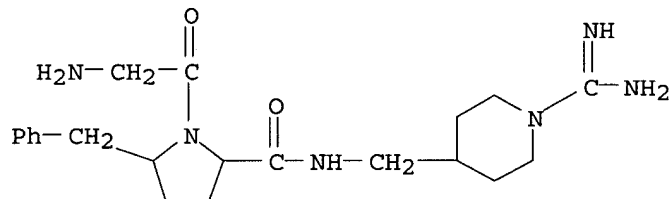
RN 199611-98-8 CAPLUS

CN Prolinamide, glycyl-N-[4-[(aminoiminomethyl)amino]butyl]-5-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 199611-99-9 CAPLUS

CN Prolinamide, glycyl-N-[[1-(aminoiminomethyl)-4-piperidinyl]methyl]-5-(phenylmethyl)- (9CI) (CA INDEX NAME)



L51 ANSWER 40 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:849920 CAPLUS

DOCUMENT NUMBER: 123:275214

TITLE: Structure-Activity Study of Tripeptide Thrombin Inhibitors Using α -Alkyl Amino Acids and Other Conformationally Constrained Amino Acid Substitutions

AUTHOR(S): Shuman, Robert T.; Rothenberger, Robert B.; Campbell, Charles S.; Smith, Gerald F.; Gifford-Moore, Donetta S.; Paschal, Jonathan W.; Gesellchen, Paul D.

CORPORATE SOURCE: Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, 46285, USA

SOURCE: Journal of Medicinal Chemistry (1995), 38(22), 4446-53
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English
 OTHER SOURCE(S): CASREACT 123:275214

AB In our continuing effort to design novel thrombin inhibitors, a series of conformationally constrained amino acids (e.g. α -alkyl, N-alkyl cyclic, etc.) were utilized in a systematic structure-activity study of the P3, P2, and P1 positions of tripeptide arginal thrombin inhibitors. Early examples of this effort include: D-MePhe-Pro-Arg-H, Boc-D-Phg-Pro-Arg-H, D-1-Tiq-Pro-Arg-H (D-1-Tiq = D-1,2,3,4-tetrahydroisoquinolin-1-ylcarbonyl), and Boc-D-Phe-Pro-Arg-H. The current work clarifies the contribution of each residue of the tripeptide arginals toward the potent and selective inhibition of thrombin relative to that of t-PA and plasmin. The α -methylarginal modification in the P1 residue resulted in analogs which had lower potency toward thrombin while exhibiting improved selectivity. Analogs modified at the P2 site were found to be very sensitive to the conformational changes induced by variations in side chain ring size with the flexible pipecolinic acid being 2 orders of magnitude less potent at thrombin inhibition than the conformationally constrained azetidine analog. Examination of the P3 binding region indicated that α -alkylphenylglycine residues resulted in a tendency to exhibit substantial improvements in selectivity over the nonalkylated residues. Combinations of optimal P3 and P2 changes led to compds. TFA-D-Phg(α Et)-Azt-Arg-H, TFA-D-Phg(α Me)-Azt-Arg-H, Ac-D-Phg(α Me)-Azt-Arg-H, TFA-D-Phg(α Me)-Pro-Arg-H, and two α -methylarginal analogs which are clearly more selective for thrombin vs. plasmin than the nonconformationally constrained compds.

IT 169390-39-0P

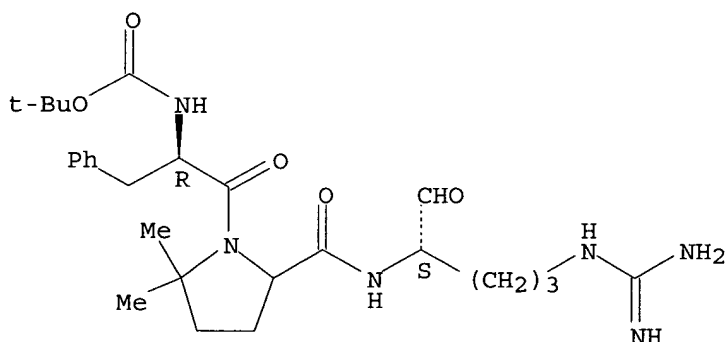
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(α -alkyl amino acids and conformationally constrained amino acids in structure-activity study of tripeptide thrombin inhibitors)

RN 169390-39-0 CAPLUS

CN Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-D-phenylalanyl-N-[4-[(aminoiminomethyl)amino]-1-formylbutyl]-5,5-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



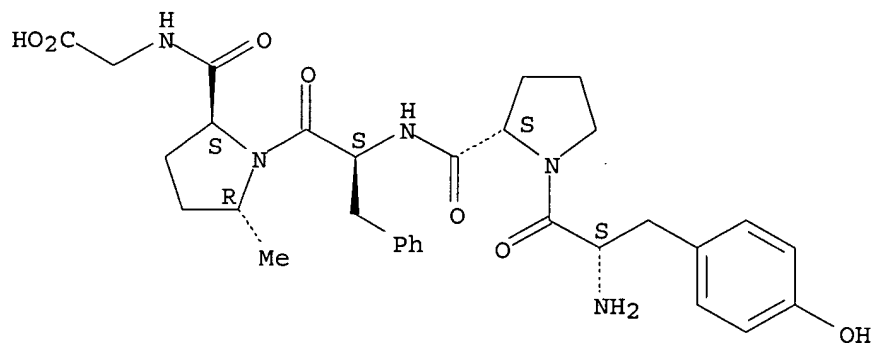
● HCl

L51 ANSWER 41 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:176125 CAPLUS
 DOCUMENT NUMBER: 122:56550
 TITLE: Synthesis of trans-5-methylproline and its influence on cis-trans isomerism in β -casomorphin-5
 AUTHOR(S): Tourwe, D.; Van Betsbrugge, J.; Verheyden, P.; Hootete, C.
 CORPORATE SOURCE: Vrije Univ. Brussel, Brussel, Belg.
 SOURCE: Bulletin des Societes Chimiques Belges (1994), 103(5-6), 201-5
 CODEN: BSCBAG; ISSN: 0037-9646
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 122:56550

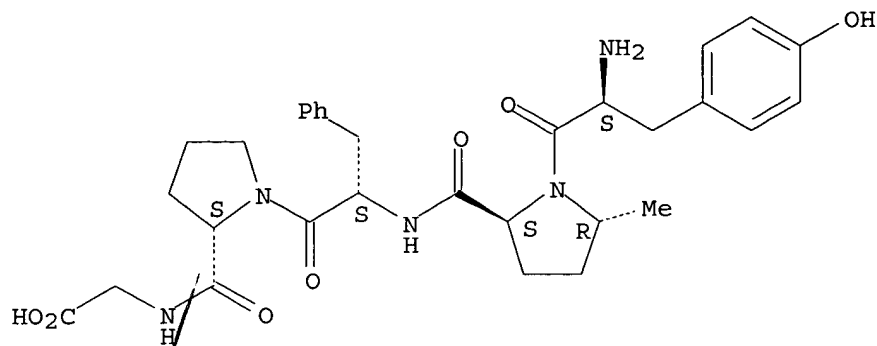
AB Starting from L-proline, trans-5-methylproline has been prepared using electrochem. oxidation followed by methylcopper substitution. After incorporation of this amino acid into β -casomorphin-5 at the two and four position, an NMR study revealed only limited influence on the cis/trans ratio of the peptide bond. The opioid receptor affinities did not allow to confirm the requirement for a cis Tyr-Pro peptide bond for biol. activity.
 IT 160033-53-4P 160033-54-5P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation of methylproline and its influence on cis-trans isomerism in β -casomorphin-5)
 RN 160033-53-4 CAPLUS
 CN Glycine, N-[trans-5-methyl-1-[N-(1-L-tyrosyl-L-prolyl)-L-phenylalanyl]-L-prolyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 160033-54-5 CAPLUS
 CN Glycine, N-[1-[N-(trans-5-methyl-1-L-tyrosyl-L-prolyl)-L-phenylalanyl]-L-prolyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 42 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:483990 CAPLUS

DOCUMENT NUMBER: 121:83990

TITLE: Preparation of peptide derivatives as thrombin inhibitors

INVENTOR(S): Teger-Nilsson, Ann Catrine Elisabet; Bylund, Ruth Elvy

PATENT ASSIGNEE(S): Aktiebolaget Astra, Swed.

SOURCE: PCT Int. Appl., 126 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

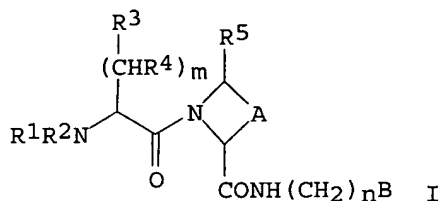
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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|---|------|----------|-----------------|----------|
| WO 9311152 | A1 | 19930610 | WO 1992-SE832 | 19921201 |
| W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, UA | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG | | | | |
| IN 180494 | A | 19980207 | IN 1992-DE1099 | 19921123 |
| ZA 9209099 | A | 19930607 | ZA 1992-9099 | 19921124 |
| AU 9331209 | A1 | 19930628 | AU 1993-31209 | 19921201 |
| AU 670052 | B2 | 19960704 | | |
| EP 618926 | A1 | 19941012 | EP 1992-924993 | 19921201 |
| EP 618926 | B1 | 20000301 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| HU 70431 | A2 | 19951030 | HU 1994-1474 | 19921201 |
| JP 09500356 | T2 | 19970114 | JP 1993-510053 | 19921201 |
| JP 3306826 | B2 | 20020724 | | |
| AT 190066 | E | 20000315 | AT 1992-924993 | 19921201 |
| CA 2125175 | C | 20010911 | CA 1992-2125175 | 19921201 |
| US 5614499 | A | 19970325 | US 1992-984884 | 19921202 |
| CN 1076199 | A | 19930915 | CN 1992-115304 | 19921204 |
| FI 9402645 | A | 19940603 | FI 1994-2645 | 19940603 |
| FI 115770 | B1 | 20050715 | | |
| NO 9402066 | A | 19940603 | NO 1994-2066 | 19940603 |
| NO 311361 | B1 | 20011119 | | |
| US 5736521 | A | 19980407 | US 1995-481810 | 19950607 |
| US 5747460 | A | 19980505 | US 1995-484426 | 19950607 |
| US 5955433 | A | 19990921 | US 1995-480818 | 19950607 |
| AU 9650616 | A1 | 19960801 | AU 1996-50616 | 19960412 |
| AU 683793 | B2 | 19971120 | | |

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A 19911204
A 19921201
A1 19921202
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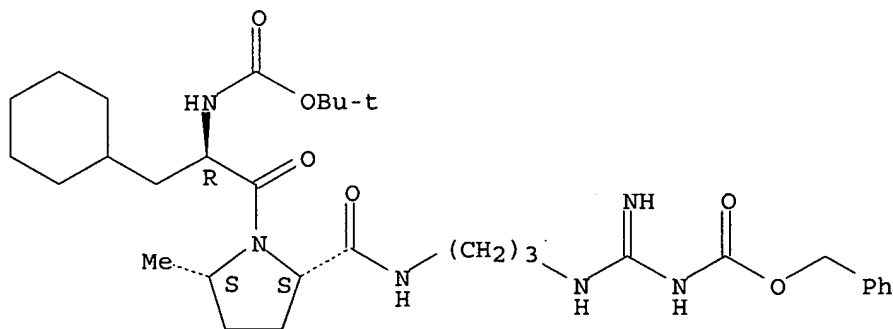
GI



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`.vative)`

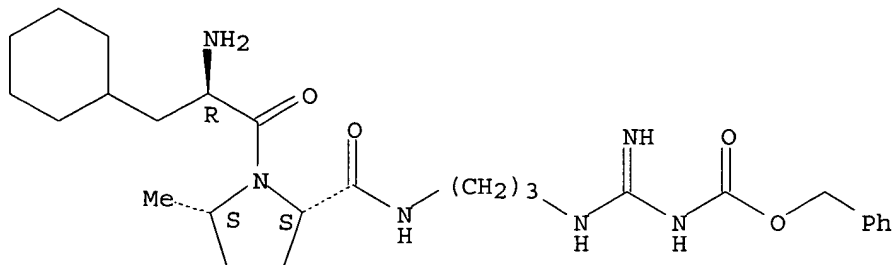
- [3



RN 155414-50-9 CAPLUS

CN L-Prolinamide, 3-cyclohexyl-D-alanyl-N-[3-[[imino[(phenylmethoxy)carbonyl]amino]methyl]amino]propyl]-5-methyl-, cis- (9CI) (CA INDEX NAME)

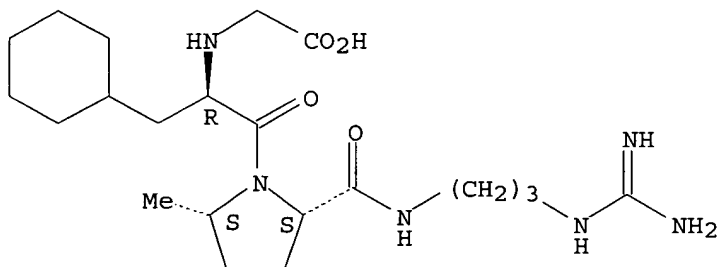
Absolute stereochemistry.

IT 155415-05-7P 155415-13-7P 155453-85-3P
155453-86-4P 155488-37-2PRL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as thrombin inhibitor)

RN 155415-05-7 CAPLUS

CN L-Prolinamide, N-(carboxymethyl)-3-cyclohexyl-D-alanyl-N-[3-[(aminoiminomethyl)amino]propyl]-5-methyl-, cis- (9CI) (CA INDEX NAME)

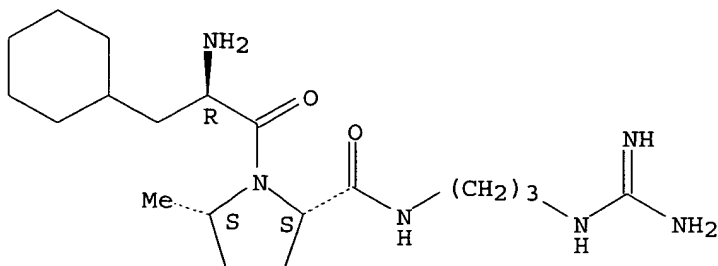
Absolute stereochemistry.



RN 155415-13-7 CAPLUS

CN L-Prolinamide, 3-cyclohexyl-D-alanyl-N-[3-[(aminoiminomethyl)amino]propyl]-5-methyl-, cis- (9CI) (CA INDEX NAME)

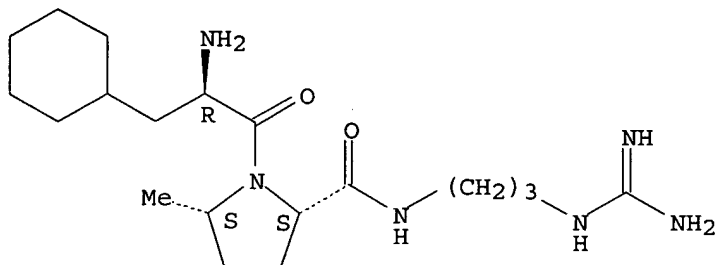
Absolute stereochemistry.



RN 155453-85-3 CAPLUS

CN L-Prolinamide, 3-cyclohexyl-D-alanyl-N-[3-[(aminoiminomethyl)amino]propyl]-5-methyl-, dihydrochloride, cis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

RN 155453-86-4 CAPLUS

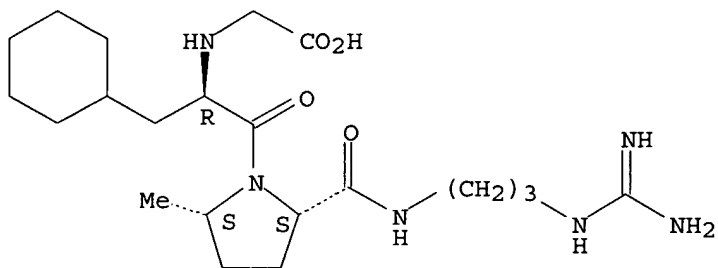
CN L-Prolinamide, N-(carboxymethyl)-3-cyclohexyl-D-alanyl-N-[3-[(aminoiminomethyl)amino]propyl]-5-methyl-, cis-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 155415-05-7

CMF C21 H38 N6 O4

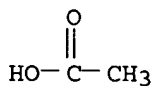
Absolute stereochemistry.



CM 2

CRN 64-19-7

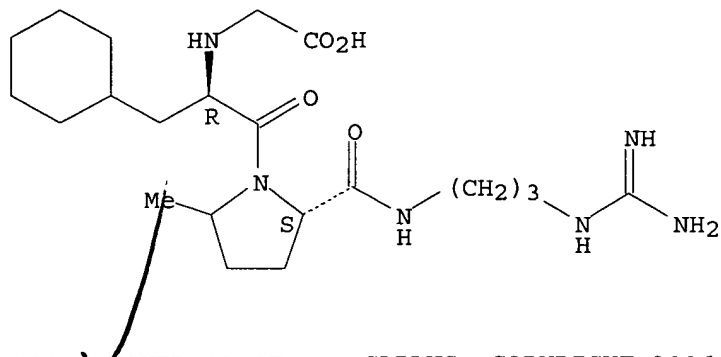
CMF C2 H4 O2



RN 155488-37-2 CAPLUS

CN L-Prolinamide, N-(carboxymethyl)-3-cyclohexyl-D-alanyl-N-[3-
[(aminoiminomethyl)amino]propyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 43 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:217658 CAPLUS

DOCUMENT NUMBER: 120:217658

TITLE: Preparation and formulation of 2- aryl-3-
(ureidoacetyl)thiazolidine-4-carboxylates and analogs
as CCK receptor and gastrin receptor ligands

INVENTOR(S): Capet, Marc; Cotrel, Claude; Guyon, Claude; Joannic,
Michel; Manfre, Franco; Roussel, Gerard; Dubroeuq,
Marie Christine; Cheve, Michel; Dutruc-Rosset, Gilles

PATENT ASSIGNEE(S): Rhone-Poulenc Rorer SA, Fr.

SOURCE: PCT Int. Appl., 186 pp.

CODEN: PIXXD2

DOCUMENT TYPE: **Patent**

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 9301167 | A1 | 19930121 | WO 1992-FR626 | 19920703 |
| W: AU, CA, CS, FI, HU, JP, KR, NO, PL, RU, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| FR 2678938 | A1 | 19930115 | FR 1991-8675 | 19910710 |
| FR 2678938 | B1 | 19931008 | | |
| EP 527069 | A1 | 19930210 | EP 1992-401904 | 19920703 |
| R: PT | | | | |
| AU 9223275 | A1 | 19930211 | AU 1992-23275 | 19920703 |
| AU 662345 | B2 | 19950831 | | |
| EP 593639 | A1 | 19940427 | EP 1992-915456 | 19920703 |
| EP 593639 | B1 | 19950405 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| JP 06509331 | T2 | 19941020 | JP 1992-502018 | 19920703 |
| JP 3034043 | B2 | 20000417 | | |
| AT 120732 | E | 19950415 | AT 1992-915456 | 19920703 |
| ES 2071510 | T3 | 19950616 | ES 1992-915456 | 19920703 |
| HU 70403 | A2 | 19951030 | HU 1994-61 | 19920703 |
| PL 171054 | B1 | 19970228 | PL 1992-313380 | 19920703 |
| PL 171094 | B1 | 19970328 | PL 1992-313379 | 19920703 |
| PL 171112 | B1 | 19970328 | PL 1992-313381 | 19920703 |
| PL 171095 | B1 | 19970328 | PL 1992-313382 | 19920703 |
| PL 171333 | B1 | 19970430 | PL 1992-302029 | 19920703 |

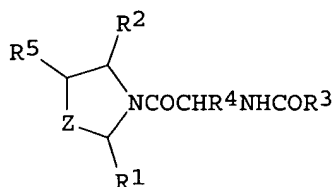
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|------------|----|----------|-----------------|----------|
| CZ 283602 | B6 | 19980513 | CZ 1994-49 | 19920703 |
| RU 2118316 | C1 | 19980827 | RU 1994-15258 | 19920703 |
| CA 2102697 | C | 20030930 | CA 1992-2102697 | 19920703 |
| ZA 9205128 | A | 19930428 | ZA 1992-5128 | 19920709 |
| NO 9304300 | A | 19931126 | NO 1993-4300 | 19931126 |
| NO 180166 | B | 19961118 | | |
| NO 180166 | C | 19970226 | | |
| FI 105190 | B1 | 20000630 | FI 1994-72 | 19940107 |
| US 5610144 | A | 19970311 | US 1994-175381 | 19940627 |

PRIORITY APPLN. INFO.:

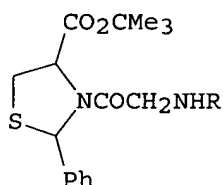
| | | |
|---------------|---|----------|
| FR 1991-8675 | A | 19910710 |
| WO 1992-FR626 | A | 19920703 |

OTHER SOURCE(S): MARPAT 120:217658

GI



I



II

AB Title compds. [I; Z = CH₂, CH₂CH₂, SOO-2, CHOH and R₁ = (substituted) (hetero)aryl; Z = CH₂, R₁ = H, and R₅ = Ph; Z = CHPh and R₁ = R₅ = H; R₂ = alkoxy carbonyl, CONH₂, Ph, etc.; R₃ = (substituted) phenylamino, Ph, etc.; R₄ = H, alkyl] were prepared. Thus, L-HSCH₂CH(NH₂)CO₂H was cyclocondensed with PhCHO and the esterified product N-acetylated with Me₃CO₂CNHCH₂CO₂H to give, after silica chromatog. and deprotection, thiazolidinecarboxylate (2R,4R)-II (III; R = H). The latter was condensed with 3-MeC₆H₄NCO to give III (R = CONHC₆H₄Me-3). I had IC₅₀ ≤ 1 mM for inhibition of binding at CCK receptors. Prepare of a chiral HPLC phase for optical resolution of I is given.

IT 153243-03-9P 153243-04-0P

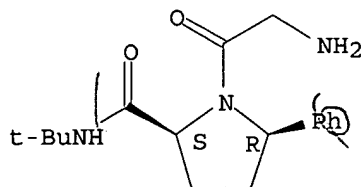
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, in preparation of CCK and gastrin receptor ligand)

RN 153243-03-9 CAPLUS

CN D-Prolinamide, glycyl-N-(1,1-dimethylethyl)-5-phenyl-, (5S)-rel- (9CI)
(CA INDEX NAME)

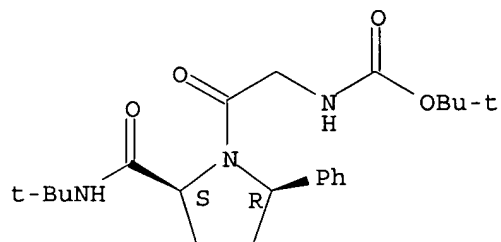
Relative stereochemistry.



RN 153243-04-0 CAPLUS

CN D-Prolinamide, N-[(1,1-dimethylethoxy) carbonyl]glycyl-N-(1,1-dimethylethyl)-5-phenyl-, (5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



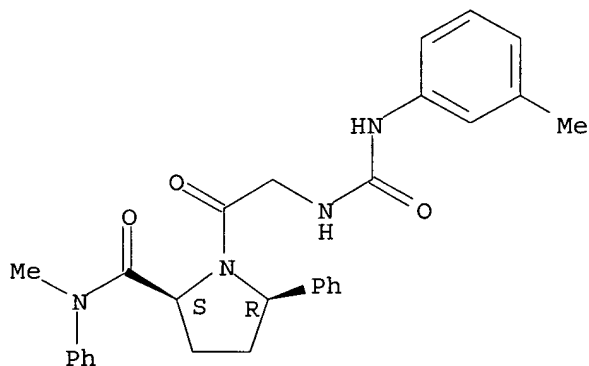
IT 153241-75-9P 153241-76-0P 153241-77-1P
153241-78-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as CCK and gastrin receptor ligand)

RN 153241-75-9 CAPLUS

CN D-Prolinamide, N-[[[(3-methylphenyl)amino]carbonyl]glycyl-N-methyl-N,5-diphenyl-, (5S)-rel- (9CI) (CA INDEX NAME)

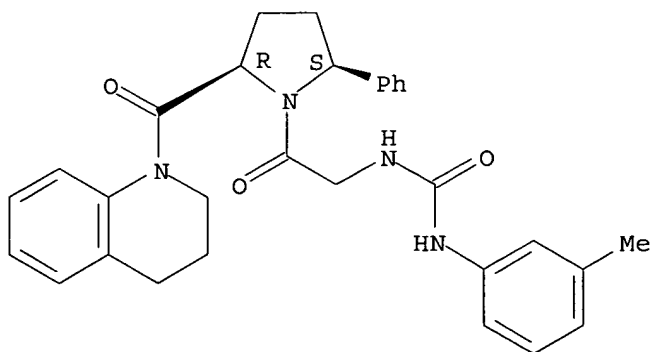
Relative stereochemistry.



RN 153241-76-0 CAPLUS

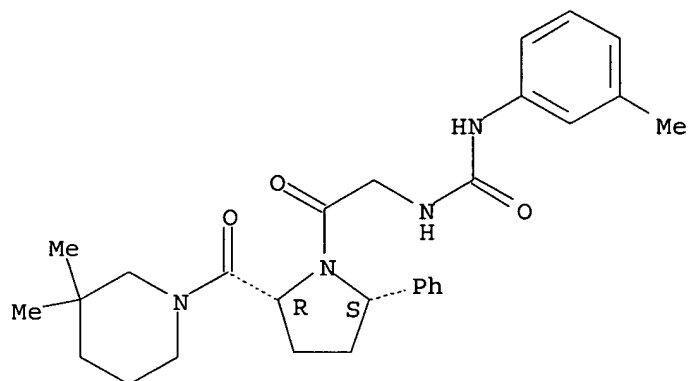
CN Quinoline, 1,2,3,4-tetrahydro-1-[[[1-[[[(3-methylphenyl)amino]carbonyl]amino]acetyl]-5-phenyl-2-pyrrolidinyl]carbonyl]-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



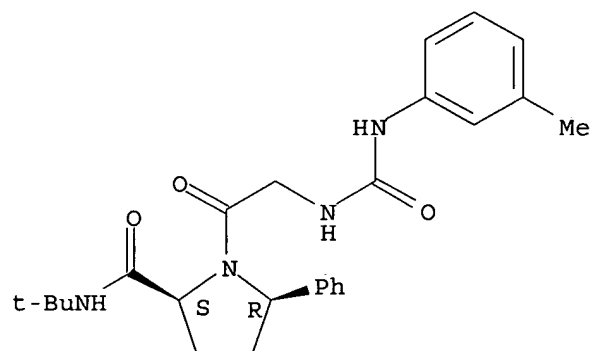
RN 153241-77-1 CAPLUS
 CN Piperidine, 3,3-dimethyl-1-[[1-[[[(3-methylphenyl)amino]carbonyl]amino]acetyl]-5-phenyl-2-pyrrolidinyl]carbonyl]-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 153241-78-2 CAPLUS
 CN D-Prolinamide, N-[[[(3-methylphenyl)amino]carbonyl]glycyl-N-(1,1-dimethylethyl)-5-phenyl]-, (5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



✓ L51 ANSWER 44 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:403890 CAPLUS

DOCUMENT NUMBER: 117:3890

TITLE: Protactin, a new antibiotic metabolite and a possible precursor of the actinomycins

AUTHOR(S): Hanada, Minoru; Sugawara, Koko; Nishiyama, Yuji; Kamei, Hideo; Hatori, Masami; Konishi, Masataka

CORPORATE SOURCE: Bristol-Myers Squibb Res. Inst., Tokyo, 153, Japan

SOURCE: Journal of Antibiotics (1992), 45(1), 20-8

CODEN: JANTAJ; ISSN: 0021-8820

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Streptomyces cucumerosporus strain L703-4 (ATCC 53784) produces a new 4-methyl-3-hydroxyanthraniloypentapeptide lactone designated protactin, in addition to several actinomycin components. Protactin is rather resistant

141912-61-0P

RN

CN

CN

CC1=CC=C(C(=C1)C(=O)NC(=O)NC(C)C)C(=O)NC(C)C(=O)O
$$\text{Me} - \text{C}_4\text{H}_4\text{N} - \text{C}(=\text{O}) - \text{N} - \text{CH}_2 - \text{C}(=\text{O}) - \text{N} - \text{CH}(\text{Pr-i})$$